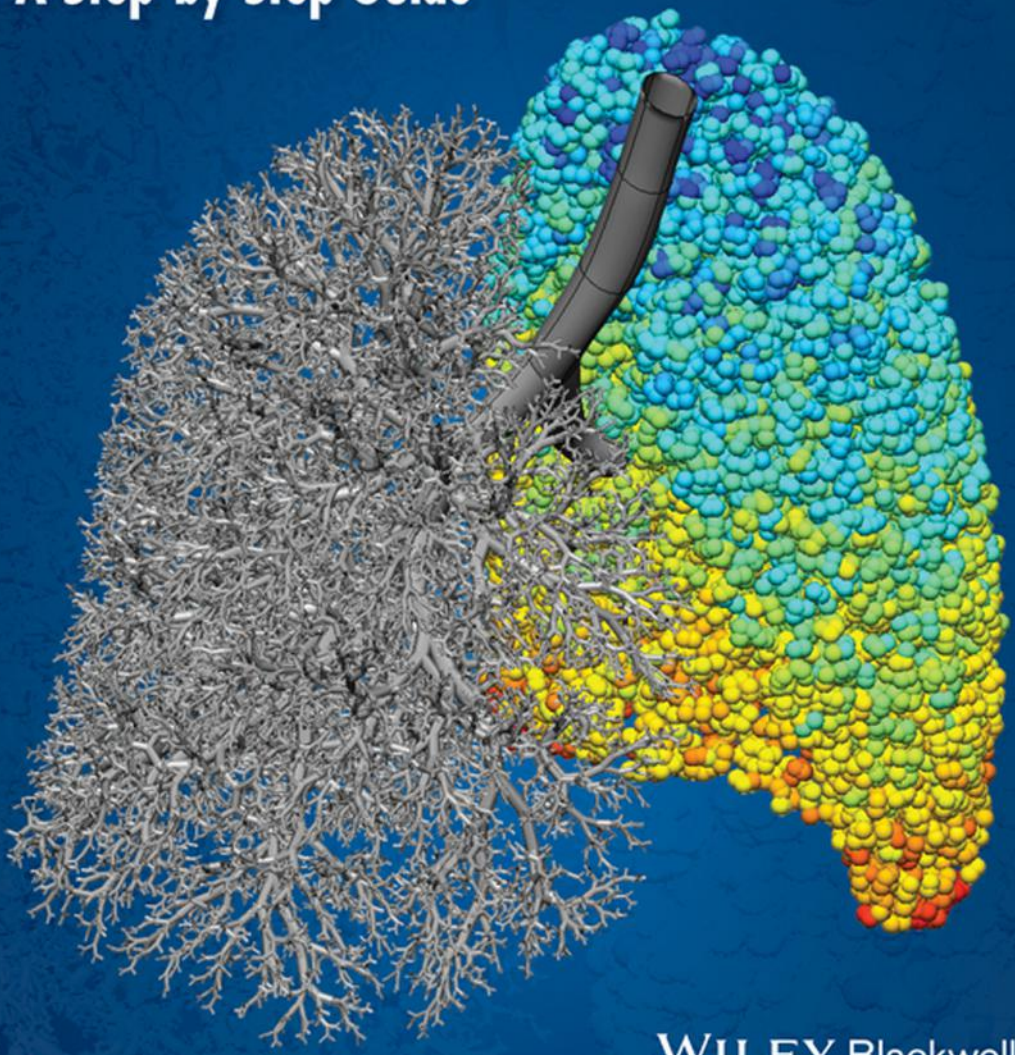
Brigitte M. Borg, Bruce R. Thompson and Robyn E. O'Hehir

Interpreting Lung Function Tests:

A Step-by-Step Guide



WILEY Blackwell

Interpreting Lung Function Tests

Interpreting Lung Function Tests

A STEP-BY-STEP GUIDE

Brigitte M. Borg, BAppSc, CRFS

Deputy Head, Physiology Service
Department of Allergy, Immunology and Respiratory Medicine
Alfred Hospital and Monash University
Melbourne, Victoria, Australia

Bruce R. Thompson, BAppSc, CRFS, PhD, FANZSRS

Professor and Head, Physiology Service
Department of Allergy, Immunology and Respiratory Medicine
Alfred Hospital and Monash University
Melbourne, Victoria, Australia

Robyn E. O'Hehir, FRACP, PhD, FRCP, FRCPath

Professor and Director
Department of Allergy, Immunology and Respiratory Medicine
Alfred Hospital and Monash University
Melbourne, Victoria, Australia

WILEY Blackwell

This edition first published 2014 © 2014 by John Wiley & Sons, Ltd.

Registered office: John Wiley & Sons, Ltd, The Atrium, Southern Gate, Chichester, West Sussex, PO19 8SQ, UK

Editorial offices: 9600 Garsington Road, Oxford, OX4 2DQ, UK
The Atrium, Southern Gate, Chichester, West Sussex, PO19 8SQ, UK
111 River Street, Hoboken, NJ 07030-5774, USA

For details of our global editorial offices, for customer services and for information about how to apply for permission to reuse the copyright material in this book please see our website at www.wiley.com/wiley-blackwell

The right of the author to be identified as the author of this work has been asserted in accordance with the UK Copyright, Designs and Patents Act 1988.

All rights reserved. No part of this publication may be reproduced, stored in a retrieval system, or transmitted, in any form or by any means, electronic, mechanical, photocopying, recording or otherwise, except as permitted by the UK Copyright, Designs and Patents Act 1988, without the prior permission of the publisher.

Designations used by companies to distinguish their products are often claimed as trademarks. All brand names and product names used in this book are trade names, service marks, trademarks or registered trademarks of their respective owners. The publisher is not associated with any product or vendor mentioned in this book. It is sold on the understanding that the publisher is not engaged in rendering professional services. If professional advice or other expert assistance is required, the services of a competent professional should be sought.

The contents of this work are intended to further general scientific research, understanding, and discussion only and are not intended and should not be relied upon as recommending or promoting a specific method, diagnosis, or treatment by health science practitioners for any particular patient. The publisher and the author make no representations or warranties with respect to the accuracy or completeness of the contents of this work and specifically disclaim all warranties, including without limitation any implied warranties of fitness for a particular purpose. In view of ongoing research, equipment modifications, changes in governmental regulations, and the constant flow of information relating to the use of medicines, equipment, and devices, the reader is urged to review and evaluate the information provided in the package insert or instructions for each medicine, equipment, or device for, among other things, any changes in the instructions or indication of usage and for added warnings and precautions. Readers should consult with a specialist where appropriate. The fact that an organization or Website is referred to in this work as a citation and/or a potential source of further information does not mean that the author or the publisher endorses the information the organization or Website may provide or recommendations it may make. Further, readers should be aware that Internet Websites listed in this work may have changed or disappeared between when this work was written and when it is read. No warranty may be created or extended by any promotional statements for this work. Neither the publisher nor the author shall be liable for any damages arising herefrom.

Library of Congress Cataloging-in-Publication Data

Borg, Brigitte M. (Marianne), 1970- author.
Interpreting lung function tests : a step-by-step guide / Brigitte Marianne Borg, Bruce Robert Thompson, Robyn Elizabeth O'Hehir.
p. ; cm.
Includes bibliographical references and index.
ISBN 978-1-118-40551-2 (pbk.)
I. Thompson, Bruce R. (Robert), 1967- author. II. O'Hehir, Robyn E. (Elizabeth), 1954- author. III. Title.
[DNLM: 1. Respiratory Function Tests. WF 141]
RC734.P84
616.2'40754 – dc23

2014005432

A catalogue record for this book is available from the British Library.

Wiley also publishes its books in a variety of electronic formats. Some content that appears in print may not be available in electronic books.

Cover image: Courtesy of Professor Merryn Tawhai and Professor Bruce Thompson

Typeset in 10/13pt Palatino by Laserwords Private Limited, Chennai, India

1 2014

Contents

About the authors, vii

Forewords, ix

Preface, xi

Acknowledgement, xiii

1 General features of interpretation and report writing, 1

2 Spirometry, 13

3 Static lung volumes, 37

4 Carbon monoxide transfer factor: single breath method, 53

5 Tests of respiratory muscle strength, 79

6 Bronchial provocation tests, 99

7 The importance of quality tests, 117

8 When the results do not fit the rules, 139

Glossary, 161

Index, 165

About the authors

Ms Brigitte M. Borg

Brigitte Borg has a Bachelor of Applied Science (Medical Biophysics and Instrumentation) and is a Certified Respiratory Function Scientist. Brigitte is the Deputy Head of the Physiology Service, Allergy, Immunology and Respiratory Medicine at The Alfred, Melbourne. She is responsible for the day-to-day management of a busy lung function laboratory that encompasses clinical, research and education in its core activities. Brigitte has actively participated in the training of advanced trainees in lung function interpretation over many years and has been on the faculty of the American Thoracic Society's postgraduate course for the Interpretation of Lung Function since 2008. Brigitte's research interests are twofold: quality of measurement of lung function and oxygen therapy.

Professor Bruce R. Thompson

Professor Bruce Thompson, B. App. Sci, CRFS, PhD, FANZSRS, is the Head of the Physiology Service within the Department of Allergy, Immunology and Respiratory Medicine, Alfred Hospital and Central Clinical School, Monash University. After graduating with a degree in Physiology and Electronics, he completed a PhD examining the effects of ventilation heterogeneity on gas transfer factor. Prof. Thompson is the head of one of the largest pulmonary function laboratories in Australia and combines a very active research programme. Prof. Thompson's research interest centres on the structure and function of the small airways, and he also has a very keen interest in quality of pulmonary function measurements. He is a member of the Global Lung Initiative T_LCO taskforce. Finally, his contribution to respiratory research and laboratory measurement was recognised in 2011 when he was awarded the ANZSRS research medal (Fellowship).

Professor Robyn E O'Hehir

Professor O'Hehir, FRACP, PhD, FRCP, FRCPath, is Professor and Director of the Department of Allergy, Immunology and Respiratory Medicine, Alfred Hospital and Central Clinical School, Monash University. After graduating in Science (Microbiology, Biochemistry and Physiology) and then in Medicine at Monash University and Alfred Hospital, Melbourne, Australia, she completed her clinical postgraduate training at Royal Brompton Hospital and the University of London, specialising in both Allergy and Clinical Immunology and Respiratory Medicine. Professor O'Hehir conducts an active programme combining clinical care, clinical and experimental research and education. She is an Editor of the international journal *Clinical and Experimental Allergy* and has a strong interest in translational medicine.

Forewords

Tell me and I forget, teach me and I may remember, involve me and I learn.

Benjamin Franklin

Franklin realised that effective teaching occurs when one involves the learner in his or her own education. We all have had memorable learning experiences when our teachers presented us with learning material or activity that was more germane to our jobs and activities. Yet scant attention has been paid to the teaching of the interpretation of lung function tests. In contrast to the vast number of books on ECG interpretation, try finding a decent book of PFT interpretation!

This book is exceptional and singular. The book is divided into eight chapters. Five of the chapters cover the five standard pulmonary function tests widely used by most lung function laboratories worldwide. However, three of the chapters deal with, first, a general approach to interpretation of lung function tests and then their report writing. The latter is the most helpful treatment I have ever seen on the topic. Next, there is a complete chapter devoted to test quality. Lastly, and perhaps uniquely, is Chapter 8 devoted to unusual test results that cause difficulties in interpretation, for example, patients with borderline results. Again, this is totally unique material.

However, the best part of this book is the number and quality of the case studies, and the best part of these is the presence of complete interpretations. Oh, what I would have given to have this book the first day I sat down with a stack of PFT results! If you spent the time on the cases, then you would make Ben Franklin proud. So take a deep breath and turn the page!

Charles G. Irvin, Ph.D.
University of Vermont
Burlington, Vermont

The lung is a highly complex organ whose access is difficult. Detection of abnormalities is largely dependent on measuring indices of lung function and imaging, other methods require invasive procedures such as bronchoscopy and tissue biopsy. Understanding how an organ with so many dichotomous components works to maintain the life-giving oxygenation and rid the body of carbon dioxide has been an enormous challenge. However, huge progress has been made in establishing structure–function relationships of the lung as an integrated complex organ and its implications when these are affected by a disease leading to an informative list of tests that can precisely identify diagnoses.

However, as with any test, interpretation depends on a clear understanding of lung physiology in health and disease, limitations of surrogate markers reflecting function and the possible pitfalls of over-interpretation. Although there have been many publications that deal with various aspects of this journey, there has not been a resource that enables the clinicians to easily interpret lung function measures in their entirety.

Brigitte Borg, Bruce Thompson and Robyn O'Hehir have achieved this remarkably well in their practical book *Interpreting Lung Function Tests: A Step-by-Step Guide* by explaining how the different tests of lung function are optimally undertaken, their implications for disease diagnosis and, importantly, how results should be reported, their clinical interpretation and limitations. A particularly valuable resource provided by this unique publication is a series of well-illustrated cases illustrating how far the tests can be interpreted to aid in diagnosis and evolve over the life course.

The book is presented in an easily accessible format making it essential reading for all those delivering an effective pulmonary function service and respiratory physicians who utilise these tests for patient benefit. Such a concise and easily readable book will be of great value to those who both undertake and utilise lung function testing, especially those in training.

Stephen T Holgate CBE, DSc, MD, FRCP, FRCPath, FMed Sci.
Faculty of Medicine
Southampton University, UK

Preface

In the healthcare setting, the purpose of performing a lung function test is to provide information to assist clinical decision-making and management strategies. The current expectation is that those working in the field of respiratory medicine will be able to interpret physiological measurements of lung function. The inspiration for this book arose from our local need for a resource to educate our advanced trainee physicians specialising in respiratory medicine in interpretation and reporting of lung function.

What started as a local guideline developed into a book as the guideline was expanded to include the many aspects and considerations in reporting common lung function tests. Illustrative cases were also incorporated to close the gap between theory and practice in interpretation and report writing.

The aims of this book are as follows:

- To provide a teaching/reference tool for writing reports for lung function tests routinely performed in adults in clinical practice.
- To provide the reader with the skill to interpret and write a concise and informative report.
- To provide a uniform report format that can be used by multiple personnel reporting lung function tests within a service to promote consistency in reporting style.

There are many different tests of respiratory function, and it was not our objective to cover them all in this practical book. We have included the tests that are routinely performed in lung function laboratories, namely Spirometry, Static Lung Volumes, Gas Transfer Factor, Bronchial Provocation Tests, and Tests of Respiratory Muscle Strength. Similarly, we have chosen to focus on the lung function assessment of adults although some of the concepts equally apply to paediatrics.

We have utilised published literature to inform the interpretation strategies suggested in this book. In cases where published data are unavailable, we have formed interpretative strategies based on expert opinion.

Assumptions

The assessment of lung function is multifaceted. This book is not intended to be a technical manual on test performance or quality assurance nor a compendium of respiratory pathophysiology. In order to interpret lung function assessments, however, knowledge of these aspects is required and it is assumed that those using this book:

- have a general understanding of respiratory physiology related to lung function assessment;
- recognise and understand the standard parameters of lung function measurement (e.g. FEV_1, TLC);
- understand the importance of appropriately chosen reference values and the limitations of reference sets.

To keep it simple, the cases in Chapters 2 to 6 assume the following:

- Testing equipment used in the assessment of lung function has been properly maintained, calibrated and is part of a regular quality assurance programme to ensure the accuracy and precision of the device.
- Results include corrections for body temperature and water vapour pressure as required.
- Reference values used are appropriate to the subject for the case.
- Tests were performed according to published standards.
- Tests are of good quality and are a valid representation of the subject's true lung function.

The cases in Chapters 8 and 9, however, are not straightforward, but the issue is identified.

Our hope is that this book is of use in assisting individuals and laboratories to establish a consistent interpretative and/or reporting strategy that is, as far as possible, evidence based. Enjoy!

Brigitte Borg
Bruce Thompson
Robyn E O'Hehir

Acknowledgement

We would like to thank our families and colleagues for their support throughout the writing of this book.

Brigitte, Bruce and Robyn

CHAPTER 1

General features of interpretation and report writing

There are features in the interpretation of lung function tests and report writing that are common to most tests of lung function. This chapter explores these general features.

General features of interpretation

The general features of interpretation are (1)

1 assessing test validity;
2 assessing the adequacy of reference values for the particular subject;
3 determining normality or abnormality using upper and/or lower limits of normal;
4 classifying detected abnormalities based on known patterns of disease;
5 determining the severity of an abnormality;
6 comparing current and previous results to identify significant changes over time;
7 attempting to address clinical question(s) mentioned in the referral.

Assessing test validity

• Interpretation of results should begin with a review of test quality. Good test quality is important as suboptimal quality tests may impact negatively on the interpretation of results and hence on clinical decision making. Information regarding indicators of test quality is provided in the test-specific chapters and in Chapter 7.

Interpreting Lung Function Tests: A Step-by-Step Guide, First Edition.
Brigitte M. Borg, Bruce R. Thompson and Robyn E. O'Hehir.
© 2014 John Wiley & Sons, Ltd. Published 2014 by John Wiley & Sons, Ltd.

• The identification of suboptimal quality results can be gleaned from examination of the raw test data, technical comments provided by the test operator or a combination of both.
• When a suboptimal quality test is obtained, a cautionary statement identifying the magnitude and direction of the impact of the suboptimal quality results should be included in the report. For example:

> *Results should be interpreted with caution as test performance for spirometry was suboptimal due to coughing at end expiration, and may result in potential underestimation of forced vital capacity (FVC).*

Assessing the adequacy of reference values for the particular subject

• Lung function results are interpreted by comparing the obtained results to a known reference range.
• The reference range/equations chosen need to reflect the population(s) tested and the test methods used in the laboratory (1).
• The reference range used for each test, as well as the limits of the variables (e.g. age, height, weight) of the reference equations, should be known to those reporting.

If reference values are extrapolated beyond the limits of the variables (for example, a subject's age is 85 years, but the age range of the reference set used is 8–80 years), then a cautionary statement should be included as there is uncertainty regarding the validity of the reference data. For example: *Reference values for spirometry have been extrapolated for age and should be used with caution.*

• Lung function may be affected by race. Clear differences between Caucasian and African-American populations in the United States have been shown (2). Ideally, the subject's race (or the race they identify within the case of mixed race) should be taken into account in selecting appropriate reference sets. There are, however, practical issues in identifying and using appropriate reference sets for multiple races, and appropriate reference sets for some tests do not exist.

The Global Lung Initiative has published a multiethnic set of spirometry reference values (3), which goes some way to addressing the issue of race in reference values. At the time of writing, the Global Lung Initiative is working towards race-specific reference values for T_LCO also.

A useful, but less than ideal solution for this problem, is the application of a race correction factor (e.g. 0.88 for FEV_1 and FVC (forced vital capacity)) to

Caucasian reference values when testing non-Caucasian subjects (1). This method is by no means ideal and when a correction factor is applied, a cautionary statement should be used to inform the reader that the reference values have been adjusted for race. For example: *Reference values have been adjusted for race and should be used with caution*.

Determining normality or abnormality using upper and/or lower limits of normal

The normal range:

- The normal range is defined by the range in which there is confidence for inclusion of 95% of the normal population.
- The 95% confidence limits are determined using the mean predicted value (MPV) calculated from the reference equations and the residual standard deviation (RSD) that describes the amount of scatter or variation around the MPV.
- The upper limits of normal (ULN) and lower limits of normal (LLN) can be calculated using the MPV and the RSD as follows:
  - For parameters that may have an abnormally high or low result (e.g. haemoglobin), the upper and lower 95% confidence limits are given by
    - ULN: MPV + 1.96RSD
    - LLN: MPV – 1.96RSD
    - The limits are set at the 2.5th and 97.5th percentiles (5% in total lie outside the normal range)
  - For parameters where it is possible to have only abnormally low results (e.g. FEV_1, FVC), the lower 95% confidence limit is given by
    - LLN: MPV – 1.64RSD
    - The lower limit is set at the 5% percentile (5% lie below the normal range)
  - For parameters where it is possible to have only abnormally high results (e.g. RV (residual volume):TLC (total lung capacity) ratio), the upper 95% confidence limit is given by
    - ULN: MPV + 1.64RSD
    - The upper limit is set at the 95th percentile (5% lie above the normal range)
- A *z*-score expresses the number of standard deviations a measured result is from the mean and is calculated (measured value – MPV)/RSD. *z*-score values below the MPV are recorded as a negative number and values above the MPV as a positive number.

Using the 95% confidence limits to set the upper and/or lower limits of normal.

— Parameters that may have an abnormally low or high result: an abnormal result can be identified by a *z*-score either less than −1.96 or greater than +1.96, respectively.

— Parameters with only abnormally low results: an abnormal result can be identified by a *z*-score less than −1.64.

— Parameters with only abnormally high results: an abnormal result can be identified by a *z*-score greater than +1.64.

Determining normality or abnormality

- Limit the number of parameters used in the interpretation of lung function. The more parameters that are included in the test analysis, the more likelihood there is of returning an abnormal finding.
- When results are within normal limits, they should be reported as being *within normal limits* rather than being normal. There may be lung disease present that has not as yet forced any parameters of lung function outside the normal limits.
- When a result is abnormal, it is described as being reduced if it is below the LLN or elevated if it is above the upper limit of normal.
- Borderline results require careful consideration in interpretation and it is acceptable to describe a result as borderline.
- As the normal range is defined as the range in which there is confidence that 95% of the normal population will be included, 5% of the normal population will have an abnormal finding. This is a particularly important consideration when lung function is being tested in a general population in the absence of symptoms (e.g. pre-employment medicals, epidemiological surveys). In a doctor referred population dictated by specific symptoms, an abnormal finding is more likely to be a true abnormal finding.

Classifying detected abnormality based on known patterns of disease

- When an abnormality is identified, the pattern of abnormality should be identified.
- Ensure that information is used from all the tests performed to inform the overall interpretation of the result. For example, when spirometry and static lung volumes are performed, they should be used together to determine the pattern of abnormality as they both measure aspects of ventilatory function.
- Lung function is rarely, if ever, used as a diagnostic tool in isolation. Lung function results are usually incorporated into the larger clinical

picture (patient history, imaging, blood tests, biopsies, etc.) to assist with making a diagnosis. Suggesting a specific diagnosis based only on abnormalities of lung function is unwise as a pattern of abnormality seen in lung function results may include multiple diseases/disorders. For example:

— An obstructive ventilatory defect may be present in asthma, chronic bronchitis, emphysema, cystic fibrosis, bronchiectasis or other disorders of the airways. Differentiation cannot be made between these disorders with spirometry alone. Hence, we can only describe a pattern and not specify a diagnosis.

In the report, describe the patterns of abnormality rather than suggest specific diagnoses. For example:

— The clinical notes in a referral state, *Chronic obstructive pulmonary disease (COPD)? Extensive smoking history*. The results show an obstructive pattern with no significant response to inhaled bronchodilator. This might be reported as *There is an obstructive ventilatory defect with no significant bronchodilator response. The result is consistent with the spirometric definition of COPD*.

Determining the severity of an abnormality

• Severity scales for grading abnormal tests of spirometry and carbon monoxide transfer factor are available (Tables 1.1–1.3)(1, 4). These scales are based on arbitrary cut-offs and do not reflect functional status. For example:

An FEV_1 of 62% MPV constitutes moderate lung disease (Table 1.1). This level of lung function may impact significantly on the functional status for one person, but not for another.

• Severity scales are not recommended due to the arbitrary nature of the cut-offs. Instead, an abnormal finding should simply be called an abnormal finding. It is recommended that those who do wish to grade severity in their practice use available published scales (1, 4) for consistency (Tables 1.1–1.3). A cautionary statement should be made when using arbitrary severity scales. For example:

> *The severity scale used is arbitrary and is not necessarily representative of functional status.*

Comparing current and previous results to identify significant changes over time

Once the first result of a subject is recorded, progress is monitored by comparing current results to previous results. That is, the subject becomes their own control.

Table 1.1 Severity scale for any spirometric abnormality (1).

Adapted and reproduced with permission of the European Respiratory Society: *Eur Respir J November 2005 26:948-968; doi:10.1183/09031936.05.00035205*

Severity classification	*FEV_1 % MPV*
Mild	>70
Moderate	60–69
Moderately severe	50–59
Severe	35–49
Very severe	<35

Table 1.2 Severity scale for obstruction on spirometry using FEV_1 *z*-score (4).

[a]LLN, lower limit of normal.

Reproduced with permission of the European Respiratory Society: *Eur Respir J erj00863-2013; doi:10.1183/09031936.00086313*

Severity classification	*FEV_1/(F)VC < LLN[a] and FEV_1 z-score*
Mild	>−2
Moderate	Between −2.5 and −2
Moderately severe	Between −3 and −2.5
Severe	Between −4 and −3
Very severe	<−4

Table 1.3 Severity scale for an abnormally low carbon monoxide transfer factor (1).

[a]LLN, lower limit of normal.

Adapted and reproduced with permission of the European Respiratory Society: *Eur Respir J November 2005 26:948-968; doi:10.1183/09031936.05.00035205*

Severity classification	*T_LCO % MPV*
Mild	>60% and <LLN[a]
Moderate	40–60%
Severe	<40

- The coefficient of repeatability (CR) can be used to determine whether a change seen over time is a clinically significant change or simply due to measurement variability.
  - — From studies collecting repeated measures of lung function in healthy subjects over time, the CR is calculated as two times the standard deviation of the differences between measures. In total, 95% of observations (the difference in value of a parameter across two occasions) should fall within this range and are considered to be within the variability of the measurement. A result (the difference in value of a parameter across two occasions) that exceeds the CR is

likely to be clinically significant as it is outside of the variability of the measurement.

— At the time of writing, there are few data available in the literature to establish the CR for parameters of lung function such as FEV_1, FVC and T_LCO. Laboratory biological controls can be used to track the CR of chosen tracked parameters to set limits for significant change (1).

• Limit the number of parameters used for monitoring changes to FEV_1, (F)VC and T_LCO. Other parameters may be monitored for change, but there is increased potential for false-positive results as the likelihood of identifying a change in time increases with the increasing number of parameters monitored.

• Where measurements are made at baseline and post-bronchodilator, comparisons over time should be made between post-bronchodilator results because

— comparisons between 'best' results should be made,

— baseline conditions may vary (for example, no recent short-acting bronchodilator on one visit, but short-acting bronchodilator within 4 h on another visit).

• When making comparisons to previous results, look at the most recent previous test *AND* test results further back.

— Sometimes, there may have been no significant change from the immediate previous result, but over the prior 6–12 months there has been a significant change (improvement or decline) in FEV_1, (F)VC or T_LCO.

— For subjects who are tested infrequently (i.e. years between visits), it may also be necessary to take into account changes due to normal lung ageing. We know, for example, that FEV_1 and FVC decline as age increases once we have reached peak lung function somewhere between 20 and 25 years of age. Studies suggest that in healthy individuals, a loss in volume of up to 30 mL in FEV_1 and FVC per year is possible (5–7).

• Monitoring changes in lung function over multiple visits, rather than just two, and plotting data will also assist with identifying changes that are real (Figure 1.1).

• A change that is within the CR should be documented as 'no significant change' rather than 'no change' as there may be change, which cannot be differentiated from the variability of the measurement.

• The referring physician, who knows the timing of interventions, is the most appropriate person to interpret change over time. For example:

A finding of no significant change over a specific time is clinically important in the case of a subject with asthma who is having their inhaled

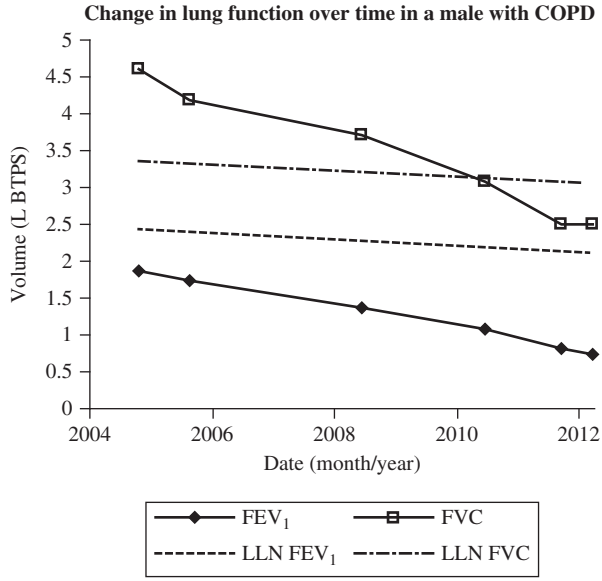


Figure 1.1 In this case, both FEV_1 and FVC appear to be changing more rapidly than expected with normal lung ageing, suggesting a significant change in ventilatory function over time. This case also illustrates no significant change in FVC between the two most recent visits, but a significant fall in FVC between the last and third last visit.

corticosteroid dose back-titrated. The reporter may not be aware of changes in management of disease.

Answering clinical question(s) raised in the referral

• Using the clinical notes, provide some clinical context to the interpretation or recommend further investigations to assist with answering the clinical question. This last step is difficult when the reporter is not the referring physician and has limited or no clinical information to aid in the interpretation. Usually the referring physician is the best individual to form the clinical context based on the 'technical' interpretation and the available clinical information.

General features of report writing

The report that accompanies the lung function results needs to be concise, informative and, where possible, address the clinical question (1). For example, consider the following case:

Gender:	Female		
Age (yr):	42	Weight (kg):	60
Height (cm):	158	Race:	Caucasian
Clinical notes:	Asthma. For review.		

	Normal range	Baseline	*z*-score	Post-BD	Change (%)
Spirometry					
FEV_1 (L)	>2.26	2.74	−0.21	2.85	+4
FVC (L)	>2.80	3.55	+0.24	3.54	0
FEV_1/FVC (%)	>72	77	−0.79	81	
Technical comment:		Test performance was good. No bronchodilator use in last 12 h.			

Without worrying too much about how the interpretation was arrived at, a report could be written a number of ways. For example:

1 NAD (no abnormality detected).

2 Spirometry is normal.

3 Spirometry is within normal limits.

4 The test is of good quality. Spirometry is within normal limits.

5 The test is of good quality. Baseline spirometry is within normal limits. There is no response to inhaled bronchodilator.

6 The test is of good quality. Baseline spirometry is within normal limits. There is no response to inhaled bronchodilator. Asthma appears to be currently well controlled, though clinical correlation is required.

Although each example is concise and correct, with increasing number, each example provides more relevant information than those before. The more relevant the information that is given to the referring doctor, the better placed he or she is to make decisions regarding clinical care.

Technical interpretation versus clinical context

Report writing consists of two aspects: technical interpretation and clinical context.

Technical interpretation:

- Can generally be performed without knowledge of the clinical history of the subject.
- Notes the quality of the test performance and the effect of suboptimal quality tests on interpretation.
- Notes appropriateness of reference values used (where necessary).
- Identifies emerging patterns of normality or abnormality.

- See report 5 in the example earlier for a written report with a technical interpretation only.
- Note: The technical interpretation is not to be confused with the technical comment, which is provided by the test operator at the time of the test and addresses any technical issues that may affect the quality and interpretation of the result.

The clinical context:

- Includes the technical interpretation.
- Is reliant on considerable clinical information about the subject being available to the reporter.
- Should be attempted in order to address the clinical question posed in the referral. However, without the necessary clinical information, specific diagnoses based on lung function tests alone should be avoided.
- Is best provided by the referring physician who has the relevant clinical information available. In this case, it is assumed that the referring doctor also has the skills and knowledge to interpret lung function results.
- Report 6 in the example earlier addresses the clinical context considering the clinical notes that have been provided.

Subjectivity

Interpretation of lung function has an element of subjectivity associated with it. Subjectivity in interpretation and report writing may impact the clinical management and care of a subject. The challenge, therefore, is to keep the degree of subjectivity in interpretation and report writing to a minimum.

Reasons for subjectivity include the following:

- The personal opinions and beliefs of the individual writing the report.
- Diversity in the literature for interpretation strategies for some tests.
- Lack of data in the literature for interpretation of particular tests or parameters within tests.
- Knowledge of the clinical background of the subject.

Strategies for reducing subjectivity include the following:

- Utilisation of published interpretation strategies where available.
- Within institutions, agreeing on interpretation strategies for tests lacking published guides or with diverse strategies in published guides.
- Requiring that all reporting personnel within an institution utilise a single, standardised lung function interpretation strategy and use similar reporting phrases – particularly for the technical interpretation.

Where possible, existing interpretation guidelines have been followed for the tests described in this book. However, there are instances where

definitions and interpretative strategies do not exist, and in these cases expert opinion has been used to create a strategy.

Summary

1 The written report should provide concise, clear and useful information regarding the test results (1).

— Keep subjectivity to a minimum.

2 Reports should include two components, ideally:

a. A technical interpretation – notes quality and inadequacies of reference equations, where applicable. Use known patterns of abnormality to classify any observed abnormalities.

b. The clinical context – using the clinical notes, provide some clinical context to the technical interpretation or recommend further investigations to assist with answering the clinical question.

References

1 Pellegrino R, Viegi G, Brusasco V, Crapo RO, Burgos F, Casaburi R, et al. Interpretative strategies for lung function tests. Eur Respir J. 2005 Nov; 26(5):948–68.

2 Hankinson JL, Odencrantz JR, Fedan KB. Spirometric reference values from a sample of the general U.S. population. Am J Respir Crit Care Med. 1999 Jan; 159(1):179–87.

3 Quanjer PH, Stanojevic S, Cole TJ, Baur X, Hall GL, Culver BH, et al. Multi-ethnic reference values for spirometry for the 3-95-yr age range: the global lung function 2012 equations. Eur Respir J. 2012 Dec; 40(6):1324–43.

4 Quanjer PH, Pretto JJ, Brazzale DJ, Boros PW. Grading the severity of airways obstruction: new wine in new bottles. Eur Respir J. 2013 Aug; 43(2):505–12.

5 Xu X, Laird N, Dockery DW, Schouten JP, Rijcken B, Weiss ST. Age, period, and cohort effects on pulmonary function in a 24-year longitudinal study. Am J Epidemiol. 1995 Mar; 141(6):554–66.

6 Speizer FE, Tager IB. Epidemiology of chronic mucus hypersecretion and obstructive airways disease. Epidemiol Rev. 1979; 1:124–42.

7 Fletcher C, Peto R. The natural history of chronic airflow obstruction. Br Med J. 1977 Jun; 1(6077):1645–8.

CHAPTER 2

Spirometry

Spirometry is probably the most commonly performed lung function test. Spirometry measures flow and volume components of ventilatory function and is measured under relaxed or forced conditions. Forced vital capacity (FVC) manoeuvres provide information regarding dynamic changes in lung volumes, whereas relaxed (slow vital capacity, SVC, or vital capacity, VC) manoeuvres provide information regarding volumes under relaxed, resting conditions.

This chapter focuses primarily on FVC manoeuvres, although SVC manoeuvres are used in the assessment of ventilatory function, static lung volumes and diaphragm function, and are mentioned throughout the book.

Test quality

The validity of spirometry results is dependent on the quality of each effort. The guidelines for spirometry state that an optimal quality result consists of a minimum of three acceptable efforts, and of these efforts, the highest and second highest FEV_1 and the highest and second highest FVC are within 150 mL (1). Test acceptability has many components, the basics of which are explained in Figure 2.1. A suboptimal quality test has the potential to affect the measured parameters of spirometry and hence impact negatively on interpretation (Figure 2.2).

Interpretation strategy

The primary parameters used in the interpretation of spirometry, in order, are as follows:

1 FEV_1/(F)VC – the ratio of FEV_1 to FVC or VC

Interpreting Lung Function Tests: A Step-by-Step Guide, First Edition.
Brigitte M. Borg, Bruce R. Thompson and Robyn E. O'Hehir.
© 2014 John Wiley & Sons, Ltd. Published 2014 by John Wiley & Sons, Ltd.

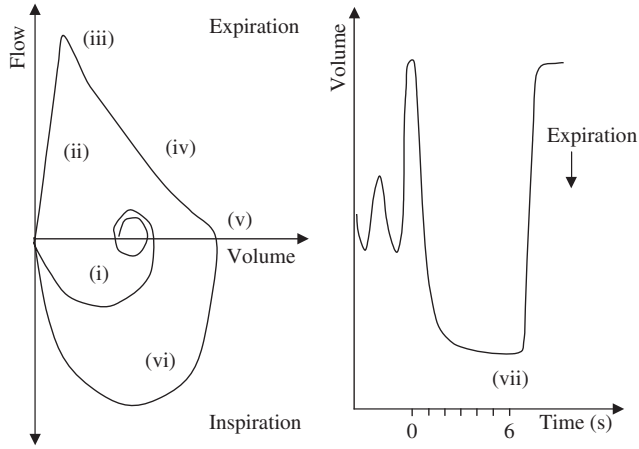


Figure 2.1 Following a maximal inspiration to total lung capacity (TLC) (i), there is a maximal, rapid exhalation, without hesitation (ii) defined by a sharp peak (iii), followed by a smooth continuous curve (iv) to a point of zero flow (or near zero flow) on the flow–volume curve (v). The inspiratory loop from residual volume (RV) back to TLC is rapid and of maximal effort (vi). The end of test criteria (no volume change for at least 1 s and 'tried to blow' for at least 6 s [3 s for children]) are best identified from the volume–time curve (vii). The peak expiratory flow (PEF) is useful for assessing the initial (blast) effort (iii).

2 (F)VC – the FVC or VC

3 FEV_1 – the forced expiratory volume in 1 s

Note: (F)VC means that either FVC or VC can be used. If both FVC and VC are measured in a test, then the largest VC is used. The largest VC can be taken from spirometry (FVC or SVC), T_LCO (V_I) or static lung volume (VC) measurements.

Other parameters of spirometry

You may notice that many testing devices list multiple parameters of spirometry in their default reports. Parameters such as PEF and FET are of benefit in assessing the quality of spirometry performance, but are not necessary for interpretation. Forced expiratory flow $(FEF)_{25–75}$ was historically used to describe small airway function. However, evidence now suggests that $FEF_{25–75}$ is not specific for small airways function in individuals and, therefore, it is no longer recommended for use in interpretation (2).

Increasing the number of parameters used in interpretation increases the chances of returning an abnormal finding, so it is best to use only FEV_1/(F)VC, (F)VC and FEV_1 for interpretation of spirometry.

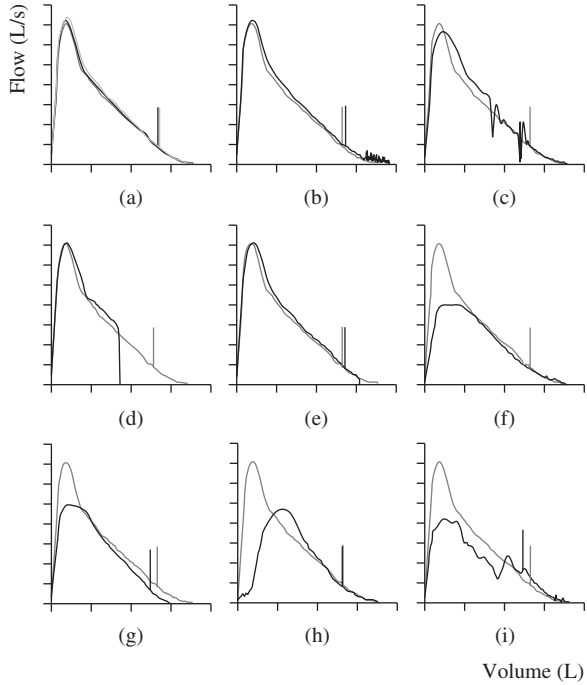


Figure 2.2 A series of expiratory flow–volume curves depicting various poor quality manoeuvres overlayed with a good quality manoeuvre. The short vertical line on the curve represents the FEV_1, and the FVC is represented by the point at which the curve touches the volume axis. (a) represents a good quality FVC manoeuvre; (b) and (c) represent FVC manoeuvres with cough, though in (b) the cough probably does not affect the validity of the test result as it occurs after 1 s, while in (c), the cough occurs before the first second and will impact on results; (d) and (e) represent glottic closure that affect FEV_1 (d only) and FVC; (f) represents a submaximal effort; (g) represents a poor lip seal and leak; (h) represents a slow start to the test and (i) represents tongue obstruction in the mouthpiece. Note how each of the suboptimal quality manoeuvres may affect the FEV_1 and FVC measurements.

Limits of normal

Lung pathology almost exclusively results in abnormally low results for parameters of spirometry used in interpretation. Hence, only a lower limit of normal is used and this is set at −1.64 *z*-scores.

Ventilatory defects can be broadly classified into obstructive, restrictive, mixed obstructive/restrictive defects and non-specific ventilatory patterns (Table 2.1) (2, 3). You will note that spirometry parameters alone are used to define results that are within normal limits or obstructive defects. Total lung capacity (TLC) measured by static lung volumes, however, is required for identifying restriction, mixed obstructive/restrictive defects and non-specific ventilatory patterns in addition to spirometry

Table 2.1 Classification of ventilatory function patterns.

Parameter	*Ventilatory pattern*
FEV_1/(F)VC, (F)VC, FEV_1 > LLN	Within normal limits
FEV_1/(F)VC < LLN	Obstructive ventilatory defect
FEV_1/(F)VC > LLN *and* TLC[a] < LLN	Restrictive ventilatory defect
FEV_1/(F)VC *and* TLC[a] < LLN	Mixed obstructive/restrictive ventilatory defect
FEV_1/(F)VC > LLN, TLC[a] > LLN, (F)VC < LLN *and/or* FEV_1 < LLN	Non-specific ventilatory pattern

[a]TLC is measured via static lung volumes.

parameters. This is because (F)VC can be reduced in spirometry due to airflow limitation or reduced lung size (Figure 2.3) and, without measuring TLC, the cause of the reduced (F)VC cannot be determined (4).

Obstructive ventilatory defects are primarily related to pathologies that result in airway narrowing (Table 2.2). Restrictive ventilatory defects (reduced lung volume) may result from pathologies intrinsic or extrinsic

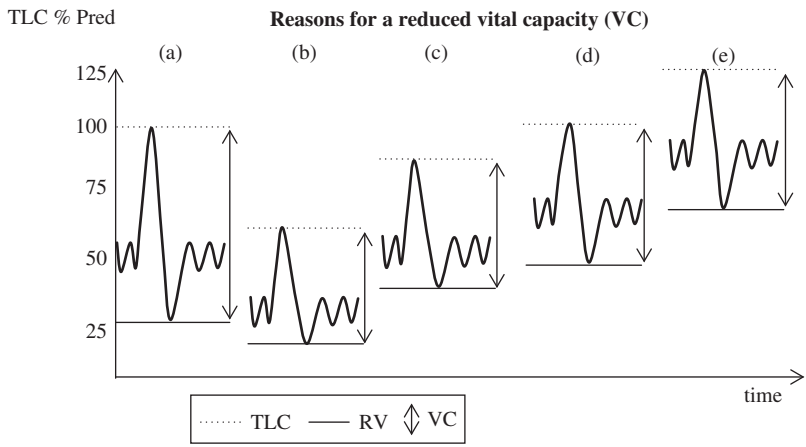


Figure 2.3 Depiction of (a) a normal trace with RV ~25% of the TLC and (b) a restrictive ventilatory pattern. RV is reduced in proportion to the reduction in TLC. VC is reduced as a result of the reduced TLC; (c) depiction of suboptimal effort or possible neuromuscular weakness. TLC is reduced and RV is elevated, resulting in a reduced VC. FRC is within the normal range; (d) depiction of obstruction with gas trapping. TLC is within the normal range but RV is elevated, with the VC reduced as a result of the elevated RV; (e) depiction of gas trapping and hyperinflation of TLC. RV is elevated disproportionately to the elevated TLC, resulting in a reduced VC.

Table 2.2 Pathologies that are reflected by obstructive or possible restrictive defects on spirometry.

Obstruction	*Restriction*[a]
Any pathology that leads to narrowing of the airways, for example: • Asthma • COPD • Emphysema • Chronic bronchitis • Bronchiectasis • Cystic fibrosis • Bronchiolitis • Foreign bodies • Tumours	Diseases of the interstitium (e.g. pulmonary fibrosis) that result in reduced compliance of the lung Pulmonary congestion (e.g. oedema) Disorders of chest wall (e.g. kyphoscoliosis) Neuromuscular disease affecting respiratory muscles Lobectomy or pneumonectomy Pleural effusion Morbid obesity

[a]Note: Static lung volumes are required to confirm restriction.

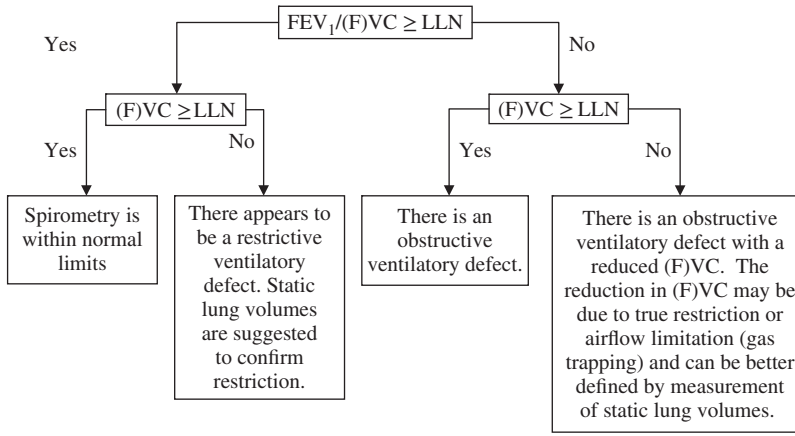

FEV1/(F)VC ≥ LLN
Yes
No
(F)VC ≥LLN
(F)VC ≥ LLN
Yes
No
Yes
No
Spirometry is within normal limits
There appears to be a restrictive ventilatory defect. Static lung volumes are suggested to confirm restriction.
There is an obstructive ventilatory defect.
There is an obstructive ventilatory defect with a reduced (F)VC. The reduction in (F)VC may be due to true restriction or airflow limitation (gas trapping) and can be better defined by measurement of static lung volumes.

Figure 2.4 Interpretation strategy using spirometry results alone.

to the lungs (Table 2.2). It is also possible that individuals may present with concomitant obstruction and restriction, resulting in a mixed obstructive/restrictive pattern. The non-specific pattern is described in more detail in Chapter 3, but is, as its name suggests, an abnormal pattern that does not fit the other defined patterns of abnormality.

The steps in interpretation using spirometry alone are shown in the flow diagram in Figure 2.4. The final level of the diagram gives an example of a written technical interpretation.

Spirometry before and after bronchodilator (BD)

• Baseline spirometry (also referred to as control or pre-bronchodilator (pre-BD) spirometry) is generally used as the basis for interpretation of spirometry.

Determining normality using post-bronchodilator spirometry should only be performed if no baseline data are recorded and this should be clearly stated. For example, *There is an obstructive ventilatory defect on post-bronchodilator spirometry* or *Post-bronchodilator spirometry shows an obstructive ventilatory defect*.

• After classifying the pattern of the baseline spirometry result, the bronchodilator response can be assessed.

Assessing bronchodilator response:

• A significant response to inhaled bronchodilator is defined as an increase ≥12% and ≥200 mL in either FEV_1 or FVC between the baseline and post-bronchodilator results (2).

— When there is a significant response to inhaled bronchodilator:

◦ If spirometry returns to within normal limits (FEV_1/(F)VC, FEV_1 and (F)VC within the normal range), then there is complete reversibility of airflow limitation.

◦ If obstruction remains apparent after inhaled bronchodilator, then there is incomplete reversibility of airflow limitation.

• Also consider responses that are insignificant by definition, but return spirometry to within normal limits and whether or not this is clinically important information.

There are a number of definitions for a significant response to inhaled bronchodilator in the literature.

Be aware of definitions that include only a percentage increase in parameters because when the baseline volume is small, a small absolute change can result in a big percentage change. The absolute change, however, may be within the variability of the measurement and may not be a real change.

Conversely, where a 12% increase in volume equates to a large absolute increase in volume (much greater than 200 mL) and the 12% change is not quite achieved, consider whether adhering strictly to the definition may result in a false-negative finding. Remember: uncertainty exists around borderline results and the term borderline can be used in reports in such cases.

Analysing the shape of the flow–volume curve

The shape of the flow–volume curve can provide information regarding the type of ventilatory defect (Figure 2.5). Be careful using the

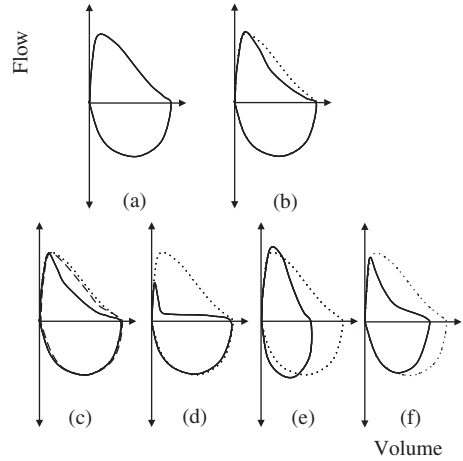


Figure 2.5 The dotted line for all curves represents a normal flow–volume curve in a young adult. (a) and (b) depict typical flow–volume curve shapes for spirometry within normal limits for a young adult and older person, respectively. Note that the expiratory limb of (b) has some concavity despite the result being within normal limits. (c) shows an example of airway obstruction with almost complete reversibility. The baseline curve (solid line) has concavity, typical of airflow obstruction. The post-bronchodilator curve (dashed line) has returned to close to the 'normal' curve (dotted). (d) depicts significant airflow obstruction. (e) represents the pattern often seen with restriction. The curve appears to be compressed along the volume axis, but the expiratory limb does not appear to have any concavity. (f) portrays an obstructive pattern. Note also that the volume appears to be reduced. This pattern may represent obstruction with a reduced FVC due to gas trapping or may represent a mixed obstructive/restrictive ventilatory pattern. Measurement of static lung volumes are required for determination.

flow–volume curve alone for identifying obstruction. The shape of the expiratory limb changes with age, and in an older population it may have a concave appearance similar to that seen in obstruction. Use the values in addition to the shape to identify the pattern seen. Also see *Special Cases of Spirometry Interpretation Upper Airway Obstruction* following for identification of upper airway obstruction using flow–volume curves.

Comparisons to previous results

- Use FEV_1 and FVC to monitor change over time.
- A change of ≥12% and ≥200 mL in either direction is likely to represent a real change over time (2).
- As explained in Chapter 1, when spirometry is measured at baseline and post-bronchodilator, comparisons over time should be made between post-bronchodilator results.

Special cases of spirometry interpretation

Upper airway obstruction

Variable or fixed upper airway obstruction is most easily identified by the shape of the flow–volume curve (also known as flow–volume loop) (Figure 2.6). Although not specific, parameters such as the FIF_{50}/FEF_{50} have been suggested to be helpful (2).

- Variable intrathoracic upper airway obstruction is characterised by flattening of the expiratory limb of the flow–volume curve (Figure 2.6b,c). $FIF_{50}/FEF_{50} > 1$ (2).
- Variable extrathoracic upper airway obstruction is characterised by a flattening of the inspiratory limb of the flow–volume curve (Figure 2.6f). $FIF_{50}/FEF_{50} < 1$ (2).
- Fixed upper airway obstruction results in flattening of both the inspiratory and expiratory limbs (Figure 2.6d,e). $FIF_{50}/FEF_{50} \sim 1$ (2).

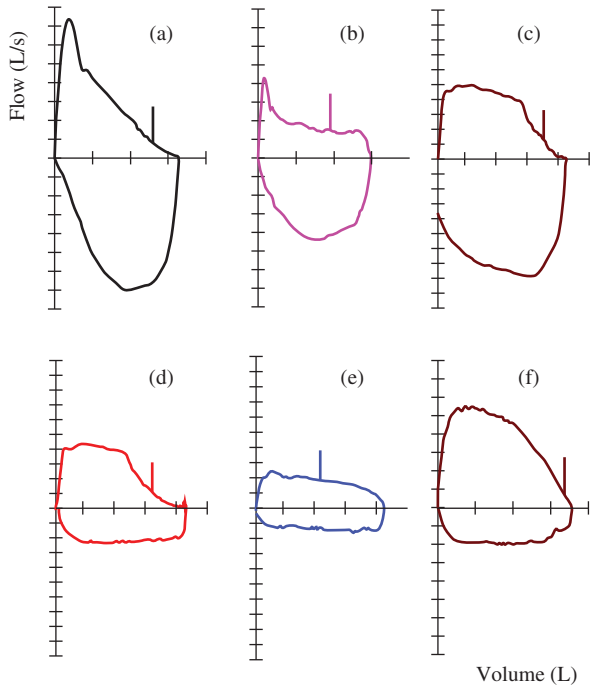


Figure 2.6 Flow–volume curve (a) depicts a normal curve shape; curves (b) and (c) are examples of variable intrathoracic upper airway obstruction; curves (d) and (e) depict examples of fixed upper airway obstruction of varying degrees; and curve (f) is an example of a variable extrathoracic upper airway obstruction.

Note:
1 FEV_1, FVC and FEV_1/FVC values may not be affected in all cases of intrathoracic airway obstruction (see Case 12). This highlights the importance of reviewing the flow–volume curves as part of the interpretation strategy.
2 In order to detect extrathoracic upper airway obstruction, a high-quality inspiratory portion of the flow–volume curve is essential. The inspiratory manoeuvre is entirely effort dependent and false-positive findings of extrathoracic upper airway obstruction can occur as a result of suboptimal effort.

Hyper-reactive airways

In a small number of individuals, the act of performing forced expiratory manoeuvres may result in progressive airways obstruction (see Case 11). The typical pattern seen with hyper-reactive airways presents as follows:
- The first effort is often within normal limits.
- The FEV_1 falls with subsequent consecutive efforts (as opposed to variable FEV_1 where changes may occur in both directions).
- Often the repeatability criteria are not met.
- Following bronchodilator, the FEV_1 may or may not return to the best baseline level, but generally post-bronchodilator FEV_1 is repeatable.

The test operator plays an important role in identifying and noting the pattern in the technical comments. It is also important that the lowest FEV_1 obtained is documented in the technical comments for reporting. The reporter should look at the raw data to confirm the pattern.

Examples of interpretation of spirometry

Spirometry interpretation is performed using the following steps as applicable:
1 Check for requirements of cautionary statements related to the following:
   a. Reference values (are values appropriate for this subject? See Chapter 1 for details).
   b. Quality of test (read technical comments, check raw data if required).
2 Read clinical notes
3 Follow flow chart of Figure 2.4
4 Assess loop shape
5 Assess response to inhaled bronchodilator
6 Write technical interpretation
7 Compare results to previous
8 Put results into clinical context.

A word about the cases

The results for each case in this book are set out in a similar format. The subject demographics appear at the top of the results, followed by clinical notes. The columns of data from left to right list the parameters measured, the normal ranges, the measured baseline values, the *z*-score of the baseline result, the measured post-bronchodilator values and finally the percentage change between the measured baseline and post-bronchodilator results. At the bottom of the results is the technical comment provided by the test operator describing the test quality and/or factors that may affect test validity.

For teaching purposes and clarity, the interpretation of the results is split into three sections: cautionary statements, technical interpretation and clinical context. The final report combines the three sections into one.

Finally, for some cases, there is a commentary providing extra information regarding the test, the results or the report.

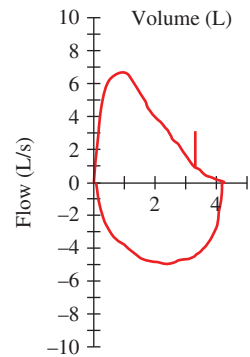
Case 1

Gender:	Male		
Age (yr):	53	Weight (kg):	78
Height (cm):	168	Race:	Caucasian

Clinical notes: Pre-surgical assessment, current smoker
80 pack years

	Normal range	Baseline	*z*-score
Spirometry			
FEV_1 (L)	>2.66	3.32	−0.04
FVC (L)	>3.55	4.27	−0.15
FEV_1/FVC (%)	>67	78	0.19

Technical comment: Test performance was good



Cautionary statements: The test is of good quality.

Technical interpretation: Baseline ventilatory function is within normal limits (*z*-scores > −1.64 for FEV_1/FVC, FVC and FEV_1).

Clinical context: No ventilatory limitation that may increase surgical risk is evident.

Final report: The test is of good quality. Baseline ventilatory function is within normal limits. No ventilatory limitation that may increase surgical risk is evident on this occasion.

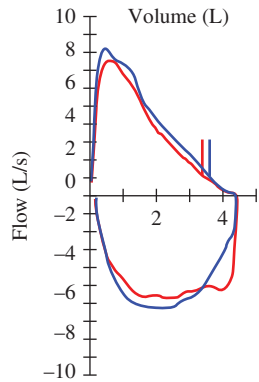
Case 2

Gender:	Male		
Age (yr):	28	Weight (kg):	53.8
Height (cm):	164	Race:	Caucasian

Clinical notes: ?asthma, never smoker

	Normal range	Baseline	*z*-score	Post-BD	Change (%)
Spirometry					
FEV_1 (L)	>3.18	3.39	−1.12	3.60	+6
FVC (L)	>3.84	4.45	−0.37	4.41	−1
FEV_1/FVC (%)	>73	76	−1.04	82	

Technical comment: Test performance was good.



Cautionary statements: The test is of good quality.

Technical interpretation: Baseline ventilatory function is within normal limits. The response to inhaled bronchodilator is not significant (although change in $FEV_1 > 200$ mL, it is <12%).

Clinical context: Asthma cannot be excluded. Consider a bronchial provocation test if clinically indicated.

Final report: The test is of good quality. Baseline ventilatory function is within normal limits. The response to inhaled bronchodilator is not significant. Asthma cannot be excluded. Consider a bronchial provocation test if clinically indicated.

Commentary: Although baseline spirometry is within normal limits and there is no response to inhaled bronchodilator, asthma cannot be excluded. The subject may not have current asthma at the time of test, for example, episodic asthma or exercise-induced asthma, or asthma may be well controlled. Ideally, any respiratory medications used prior to testing should be documented in the

technical comments (in this case, none are documented). Consideration should be given as to whether respiratory medications taken prior to the test may mask a response to inhaled bronchodilator.

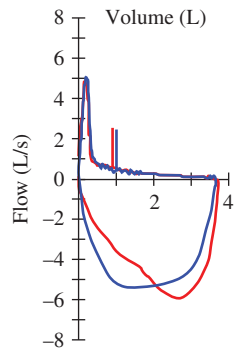
Case 3

Gender:	Male	Date:	18/4/2012
Age (yr):	79	Weight (kg):	78.4
Height (cm):	183	Race:	Caucasian

Clinical notes: COPD for review, ex-smoker 60 pack years

	Normal range	Baseline	*z*-score	Post-BD	Change (%)
Spirometry					
FEV_1 (L)	>2.34	0.93	−4.42	1.01	+9
FVC (L)	>3.43	3.57	−1.42	3.66	+3
FEV_1/FVC (%)	>62	26	−7.77	28	

Technical comment: Test performance was good.



COPD, chronic obstructive pulmonary disease.

Previous results:

	18/4/2012[a]	*17/1/2012*	*21/12/2010*	*7/5/2010*
FEV_1 (L)				
Baseline	0.93	0.93	1.01	1.15
Post-BD	1.01	0.96	1.08	1.16
FVC (L)				
Baseline	3.57	3.54	3.94	4.08
Post-BD	3.66	3.84	4.04	4.00
FEV_1/FVC (%)				
Baseline	26	26	25	28
Post-BD	28	25	27	29

[a]Current result.

Cautionary statements:	The test is of good quality.
Technical interpretation:	There is an obstructive ventilatory defect. The response to inhaled bronchodilator is not significant.
Clinical context:	Results are consistent with known COPD. In comparison to previous results from 17/1/2012 and 7/5/2010, there has been no significant change in spirometry.

Final report: The test is of good quality. There is an obstructive ventilatory defect with no significant response to inhaled bronchodilator, consistent with known COPD. In comparison to previous results from 17/1/2012 and 7/5/2010, there has been no significant change in spirometry.
Commentary: In this case, comparisons are made to previous results. The post-bronchodilator results are used for making the comparison. For FEV_1 and FVC, a change of ≥200 mL and ≥12% in either direction is considered a significant change over time. Over the short term and longer term, there has been no significant change in FEV_1 or FVC. Comparing post-bronchodilator FVC between the current result and result from 7/5/2010, although there has been a 340 mL fall in, it is not >12%.

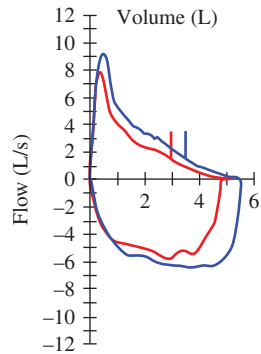
Case 4

Gender:	Male	Date:	2/3/2011
Age (yr):	55	Weight (kg):	106.9
Height (cm):	182.5	Race:	Caucasian

Clinical notes: Bronchiectasis, never smoker

	Normal range	Baseline	*z*-score	Post-BD	Change (%)
Spirometry					
FEV_1 (L)	>3.18	2.98	−2.05	3.51	+18
FVC (L)	>4.26	5.15	−0.15	5.54	+8
FEV_1/FVC (%)	>67	58	−3.20	63	

Technical comment: Test performance was good.



(*continued*)

Previous results:

	2/3/2011[a]	*6/8/2010*	*1/6/2009*
FEV_1 (L)			
Baseline	2.98		3.31
Post-BD	3.51	3.48	3.67
FVC (L)			
Baseline	5.15		5.21
Post-BD	5.54	5.59	5.43
FEV_1/FVC (%)			
Baseline	58		64
Post-BD	63	62	68

[a]Current result.

Cautionary statements: The test is of good quality.
Technical interpretation: There is an obstructive ventilatory defect. The response to inhaled bronchodilator is significant with incomplete reversibility of airflow limitation.
Clinical context: Results suggest a component of reversible airways disease. In comparison to previous results from 6/8/2010 and 1/6/2009, there has been no significant change in spirometry.

Final report: The test is of good quality. There is an obstructive ventilatory defect. The response to inhaled bronchodilator is significant with incomplete reversibility of airflow limitation. Results suggest a component of reversible airways disease. In comparison to previous results from 6/8/2010 and 1/6/2009, there has been no significant change in spirometry.

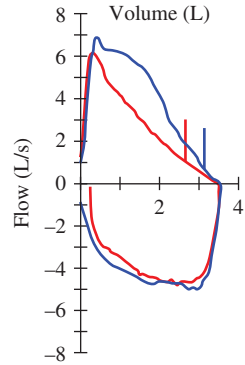
Case 5

Gender:	Female	Date:	21/2/2011
Age (yr):	20	Weight (kg):	76.65
Height (cm):	163.5	Race:	Caucasian

Clinical notes: Asthma for review, never smoker

	Normal range	Baseline	*z*-score	Post-BD	Change (%)
Spirometry					
FEV_1 (L)	>2.77	2.67	−1.91	3.14	+18
FVC (L)	>3.13	3.52	−0.72	3.56	+1
FEV_1/FVC (%)	>77	76	−1.80	88	

Technical comment: Test performance was good.



Previous results:

	21/2/2011[a]	*24/1/2011*
FEV_1 (L)		
Baseline	2.67	3.19
Post-BD	3.14	3.20
FVC (L)		
Baseline	3.52	3.54
Post-BD	3.56	3.50
FEV_1/FVC (%)		
Baseline	76	90
Post-BD	88	92

[a] Current result.

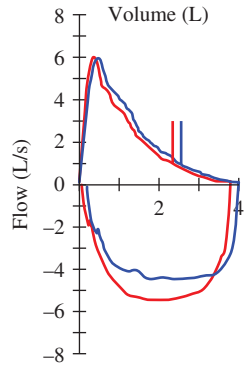
Cautionary statements: The test is of good quality.
Technical interpretation: There is an obstructive ventilatory defect. The response to inhaled bronchodilator is significant with complete reversibility of airflow limitation.
Clinical context: In comparison to previous results from 24/1/2011, there has been no significant change. Results suggest suboptimal asthma control, though clinical correlation is required.

Final report: The test is of good quality. There is an obstructive ventilatory defect. The response to inhaled bronchodilator is significant with complete reversibility of airflow limitation. In comparison to previous results from 24/1/2011, there has been no significant change. Results suggest suboptimal asthma control, though clinical correlation is required.
Commentary: Note that only post-bronchodilator data are used to make comparisons between tests. Despite baseline FEV1 having fallen 520 mL and 16%, there has not been ≥200 mL and ≥12% change in post-bronchodilator results.

Case 6

Gender:	Male		
Age (yr):	56	Weight (kg):	87.9
Height (cm):	187.5	Race:	Caucasian
Clinical notes:	COPD, current smoker 45 pack years		

	Normal range	Baseline	*z*-score	Post-BD	Change (%)
Spirometry					
FEV_1 (L)	>3.37	2.36	−3.53	2.56	+8
FVC (L)	>4.52	3.80	−2.78	3.99	+5
FEV_1/FVC (%)	>67	62	−2.45	64	
Technical comment:		Test performance was good.			



Cautionary statements:	The test is of good quality.
Technical interpretation:	There is an obstructive ventilatory defect with a reduced FVC. The response to inhaled bronchodilator is not significant. The reduction in FVC may be due to true restriction or gas trapping due to airflow limitation and can be better defined by measurement of static lung volumes.
Clinical context:	The obstruction is consistent with known COPD. FVC may be reduced due to airflow limitation-related gas trapping but true restriction cannot be excluded.

Final report: The test is of good quality. There is an obstructive ventilatory defect with a reduced FVC. The response to inhaled bronchodilator is not significant. The obstruction is consistent with known COPD. The reduction in FVC may be due to true restriction or gas trapping due to airflow limitation and can be better defined by measurement of static lung volumes.

Commentary: Remember that FVC or VC can be reduced as a result of airflow limitation or restriction. Static lung volumes are required to be able to make a determination.

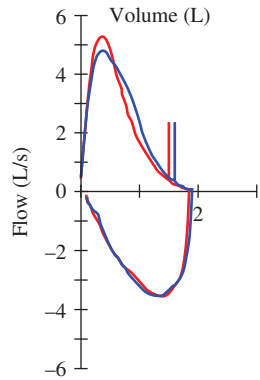
Case 7

Gender:	Female	Date:	10/1/2011
Age (yr):	70	Weight (kg):	82.5
Height (cm):	167	Race:	Caucasian

Clinical notes: For review, never smoker

	Normal range	Baseline	*z*-score	Post-BD	Change (%)
Spirometry					
FEV_1 (L)	>1.82	1.53	−2.42	1.61	+5
FVC (L)	>2.48	1.86	−3.05	1.90	+2
FEV_1/FVC (%)	>66	82	+1.06	85	

Technical comment: Test performance was good.



Previous results:

	10/1/2011[a]	*24/6/2010*	*4/5/2009*	*17/6/2007*
FEV_1 (L)				
Baseline	1.53	1.54	1.58	1.55
Post-BD	1.61	1.57	1.66	1.63
FVC (L)				
Baseline	1.86	1.97	2.00	1.95
Post-BD	1.90	1.90	2.01	1.99
FEV_1/FVC (%)				
Baseline	82	78	79	79
Post-BD	85	83	83	82

[a]Current results.

(*continued*)

Cautionary statements:	The test is of good quality.
Technical interpretation:	There appears to be a restrictive ventilatory defect. The response to inhaled bronchodilator is not significant. Static lung volumes are suggested to confirm restriction.
Clinical context:	There has been no significant change in spirometry since tests from 17/6/2007.

Final report: The test is of good quality. There appears to be a restrictive ventilatory defect with no significant response to inhaled bronchodilator. Static lung volumes are suggested to confirm restriction. In comparison to results performed since 17/6/2007, there has been no significant change in spirometry.
Commentary: In this case, there appears to be no evidence of obstruction (FEV_1/FVC is well within the normal range) and FVC is reduced. This suggests restriction may be possible, but static lung volumes are required to confirm this as the definition of restriction is a reduced TLC and FEV_1/FVC within the normal range (see Table 2.1).
Also note that no clinical notes have been provided apart from 'for review'. Hence, the only clinical context that can be provided is the comparison to previous results.

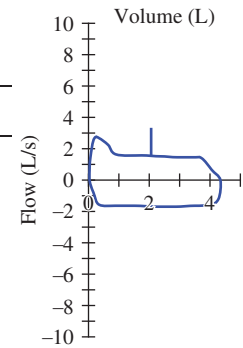
Case 8

Gender:	Female		
Age (yr):	33	Weight (kg):	65
Height (cm):	170	Race:	Caucasian

Clinical notes: Cancer of the trachea. Surgical resection 5 years ago. New tracheal stenosis, for review.

	Normal range	Baseline	*z*-score
Spirometry			
FEV_1 (L)	>2.79	2.05	−3.54
FVC (L)	>3.37	4.34	+0.46
FEV_1/FVC (%)	>74	47	−6.14

Technical comment: Test performance was good. Maximal expiratory and inspiratory loops – highly repeatable.



Cautionary statements:	The test quality is good.
Technical interpretation:	There is an obstructive ventilatory defect. Note: Flattening of both expiratory and inspiratory limbs of the flow–volume curve.
Clinical context:	Results suggest fixed upper airway obstruction, consistent with known tracheal stenosis.

Final report: The test quality is good. There is an obstructive ventilatory defect. Note: Flattening of both the inspiratory and expiratory limbs. Results are suggestive of fixed upper airway obstruction, consistent with known tracheal stenosis.

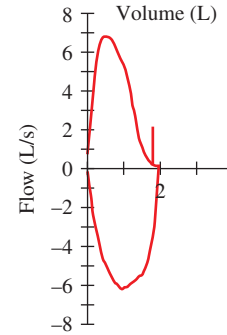
Case 9

Gender:	Male	Date:	11/4/2011
Age (yr):	63	Weight (kg):	81.8
Height (cm):	174	Race:	Caucasian

Clinical notes: ILD for review, ex-smoker 15 pack years

	Normal range	Baseline	*z*-score
Spirometry			
FEV_1 (L)	>2.56	1.80	−3.31
FVC (L)	>3.53	1.97	−4.52
FEV_1/FVC (%)	>65	91	+2.77

Technical comment: Test performance was good.



Previous results:

Baseline	*11/4/2011*[a]	*20/12/2010*	*4/10/2010*	*18/8/2010*
FEV_1 (L)	1.80	1.79	1.78	1.89
FVC (L)	1.97	1.87	1.88	2.02
VC (L)			1.95	
FEV_1/(F)VC (%)	91	96	91	94
TLC (L) (*z*-score)			2.81 (−4.91)	2.95 (−4.74)
RV (L) (*z*-score)			0.86 (−2.83)	0.91 (−2.81)
FRC (L) (*z*-score)			1.46 (−3.64)	1.47 (−3.51)

[a]Current result.

Cautionary statements: The test is of good quality.
Technical interpretation: There appears to be a restrictive ventilatory defect that has been confirmed on previous measurement of static lung volumes (4/10/2010)
Clinical context: There has been no significant change in spirometry since tests from 18/8/2010.

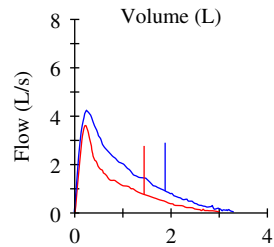
Final report: The test is of good quality. There appears to be a restrictive ventilatory defect that has been confirmed by previous measurement of static lung volumes (4/10/2010). In comparison to results obtained since 18/8/2010, there has been no significant change in FEV_1 or FVC.
Commentary: This case demonstrates the use of prior static lung volume results to assist with confirming a restrictive defect. Use caution when referring to previous static lung volume results if any of the parameters of spirometry have changed significantly between the current visit and the visit the static lung volume parameters are from. If the spirometry values have changed significantly over this time, the parameters of static lung volumes may have changed in this time also.

Case 10

Gender:	Female		
Age (yr):	52	Weight (kg):	90
Height (cm):	172	Race:	Caucasian
Clinical notes:	?asthma, never smoker		

	Normal range	Baseline	*z*-score	Post-BD	Change (%)
Spirometry					
FEV_1 (L)	>2.47	1.45	−4.20	1.90	+31
FVC (L)	>3.19	2.97	−2.12	3.29	+11
FEV_1/FVC (%)	>70	49	−5.20	58	

Technical comment: Test performance was good.



Cautionary statements: The test is of good quality.

Technical interpretation: There is an obstructive ventilatory defect with a reduced FVC. The FVC is likely to be reduced due to airflow limitation as it returns to within the normal range following inhaled bronchodilator. The response to inhaled bronchodilator is significant with incomplete reversibility of airflow limitation.

Clinical context: Results suggest that there is a reversible component to airways obstruction that is consistent with asthma. Thus, incomplete reversibility of airflow limitation indicates a fixed obstructive component also.

Final report: The test is of good quality. There is an obstructive ventilatory defect. There is a significant response to inhaled bronchodilator with incomplete reversibility of airflow limitation. Results may be consistent with asthma although other diagnoses should also be considered as there was incomplete reversibility of airflow limitation.

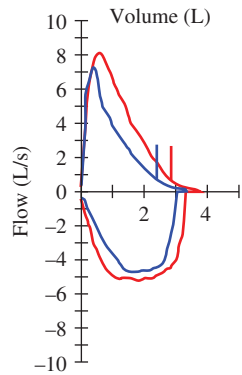
Commentary: A positive response to inhaled bronchodilator with incomplete reversibility of airflow limitation may reflect asthma or may reflect other diseases of the airways (e.g. bronchiectasis, chronic bronchitis) and these should also be considered.

Case 11

Gender:	Female		
Age (yr):	39	Weight (kg):	60
Height (cm):	165	Race:	Caucasian
Clinical notes:	Asthma. Never smoker		

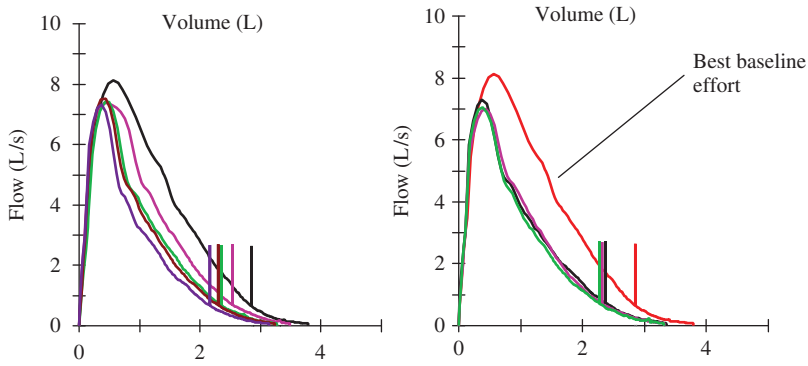
	Normal range	Baseline	*z*-score	Post-BD	Change (%)
Spirometry					
FEV_1 (L)	>2.52	2.86	−0.73	2.38	−17
FVC (L)	>3.11	3.79	−0.08	3.35	−12
FEV_1/FVC (%)	>73	75	−1.19	71	

Technical comment: Unable to meet repeatability criteria on baseline spirometry. FEV_1 fell with consecutive efforts to 2.17 L. ?Reactive airways. Test performance was good for post-bronchodilator spirometry.



Raw data

	Baseline			Post-BD		
Effort	FEV_1	FVC	FEV_1/FVC	FEV_1	FVC	FEV_1/FVC
1	2.86	3.79	75	2.38	3.35	71
2	2.55	3.48	73	2.33	3.32	70
3	2.37	3.28	72	2.28	3.32	69
4	2.31	3.24	71			
5	2.17	3.15	69			



Cautionary statements: The test quality is good, though FEV_1 and FVC fell with consecutive efforts on baseline spirometry.

Technical interpretation: Baseline ventilatory function is within normal limits. Note: Baseline FEV_1 fell with consecutive efforts to 2.17 L (24% fall in FEV_1). Following inhaled bronchodilator, spirometry did not return to best baseline levels, but was stable.

Clinical context: Possible hyper-reactive airways. Suggestive of suboptimal asthma control, though clinical correlation required.

Final report: The test quality is good. Baseline ventilatory function is within normal limits. Note: The baseline FEV_1 fell with consecutive efforts to 2.17 L (24% fall in FEV_1), suggesting hyper-reactive airways. Following inhaled bronchodilator, spirometry did not return to best baseline levels, but was stable. Results suggest suboptimal asthma control, although clinical correlation is required.

Commentary: The technical comments, in this case, point to the possibility of hyper-reactive airways. On review of the raw data, we can see that indeed FEV_1 (and FVC) drops with consecutive efforts on baseline spirometry – as the tests are individually acceptable efforts, this suggests airway hyper-reactivity. The post-bronchodilator results are repeatable (another pointer to airway hyper-reactivity), but do not return to best baseline values (in some cases of airway hyper-reactivity, the post-bronchodilator results will return to best baseline values or even surpass them).

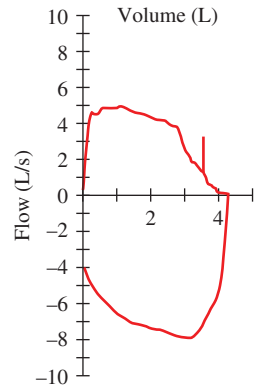
Case 12

Gender:	Male		
Age (yr):	57	Weight (kg):	100.9
Height (cm):	175.8	Race:	Caucasian

Clinical notes: Tracheomalacia. ?evidence of obstruction.

	Normal range	Baseline	*z*-score
Spirometry			
FEV_1 (L)	>2.83	3.62	0.06
FVC (L)	>3.80	4.35	−0.65
FEV_1/FVC (%)	>67	83	1.18

Technical comment: Test performance was good.



Cautionary statements: The test quality is good.

Technical interpretation: Baseline ventilatory function is within normal limits. Note: Flattening of expiratory limb of flow volume curve.

Clinical context: Although baseline lung function is within normal limits, there is flattening of the expiratory curve indicating variable intrathoracic upper airway obstruction, consistent with known tracheomalacia.

Final report: The test quality is good. Baseline ventilatory function is within normal limits; however, there is flattening of the expiratory limb of the flow volume loop, suggestive of intrathoracic upper airway obstruction. Results are consistent with known tracheomalacia.

Commentary: Although the flattening of the expiratory limb is very obvious on the flow volume curve, FEV_1/FVC, FVC and FEV_1 are all within normal limits. This illustrates the importance of reviewing flow–volume loops as part of spirometry interpretation as intrathoracic upper airway obstruction would not be picked up from reviewing the values alone in this case.

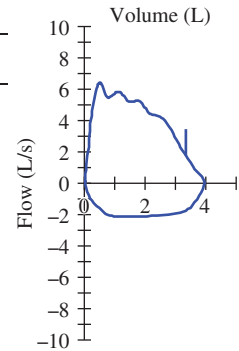
Case 13

Gender:	Male		
Age (yr):	31	Weight (kg):	52.5
Height (cm):	165.5	Race:	Caucasian

Clinical notes: Vocal cord pathology.

	Normal range	Baseline	*z*-score
Spirometry			
FEV_1 (L)	>3.16	3.31	−1.29
FVC (L)	>3.87	3.96	−1.46
FEV_1/FVC (%)	>72	84	+0.33

Technical comment: Test performance was good. Note: Consistent flattening of inspiratory loops – highly repeatable, maximal effort. Significant vocalisation on inspiration.



(*continued*)

Cautionary statements: The test quality is good.

Technical interpretation: Baseline ventilatory function is within normal limits. Note: Flattening of the inspiratory limb of the flow–volume curve. Vocalisation noted during inspiration.

Clinical context: Results suggest variable extrathoracic upper airway obstruction, which may be due to known vocal cord pathology, although clinical correlation is required.

Final report: The test quality is good. Baseline ventilatory function is within normal limits. Note: Flattening of the inspiratory limb of the flow–volume curve. Vocalisation noted during inspiration. Results suggest variable extrathoracic upper airway obstruction, which may be due to known vocal cord pathology, although clinical correlation is required.

References

1 Miller MR, Hankinson J, Brusasco V, Burgos F, Casaburi R, Coates A, et al. Standardisation of spirometry. Eur Respir J. 2005 Aug; 26(2):319–38.

2 Pellegrino R, Viegi G, Brusasco V, Crapo RO, Burgos F, Casaburi R, et al. Interpretative strategies for lung function tests. Eur Respir J. 2005 Nov; 26(5):948–68.

3 Iyer VN, Schroeder DR, Parker KO, Hyatt RE, Scanlon PD. The nonspecific pulmonary function test: longitudinal follow-up and outcomes. Chest. 2011 Apr; 139(4):878–86.

4 Aaron SD, Dales RE, Cardinal P. How accurate is spirometry at predicting restrictive pulmonary impairment? Chest. 1999 Mar; 115(3):869–73.

CHAPTER 3

Static lung volumes

Static lung volumes can be measured in the lung function laboratory by the following methods:

- Whole body plethysmography
- Multiple breath washout method
- Helium dilution method
- Single breath washout/dilution methods.

In individuals without airflow limitation, differences in measured lung volumes between methods are minimal. In obstructive disease, however, methodological differences may lead to substantial lung volume differences between methods. For example:

- Washout and dilution methods may underestimate results due to non-communicating regions in the lung being excluded from measurement.
- Plethysmography may overestimate results when the measured mouth pressure changes are not equivalent to alveolar pressure changes at zero flow. This typically occurs in the presence of substantial airway obstruction.

Test quality

Each method of measuring static lung volumes has its own particular requirements for equipment specifications, test performance and quality (1). The more general quality checks for static lung volumes include the following:

- No leak (mouth or equipment) – leak during any method of static lung volumes measurement will affect results and, as a consequence, results from trials affected by leak should not be used or reported.

Interpreting Lung Function Tests: A Step-by-Step Guide, First Edition.
Brigitte M. Borg, Bruce R. Thompson and Robyn E. O'Hehir.
© 2014 John Wiley & Sons, Ltd. Published 2014 by John Wiley & Sons, Ltd.

• Spirometry performed as part of, or separately to, the lung volume measurement should meet the spirometry requirements for acceptable and repeatable results. Failure to perform spirometry adequately can result in underestimation or overestimation of total lung capacity (TLC) and/or residual volume (RV).
• To ensure that a maximal vital capacity (VC) has been measured, the VC(L) obtained during a static lung volume measurement should be compared to the (F)VC from spirometry. Ideally, VC should be greater than (F)VC – 150 mL (where 150 mL is the repeatability criteria for VC and forced vital capacity, FVC).
• TLC obtained by static lung volume measurement should be greater than the alveolar volume (V_A) obtained during gas transfer factor (T_LCO) measurement.
• For plethysmography, three acceptable measures of functional residual capacity (FRC) within 5% of each other are required for a good quality result.
• For washout or dilution methods, often only one acceptable test is performed due to the length of time it takes for one trial to be carried out and the time required to return to normal resting conditions again. Caution should be used in interpretation of cases where only one acceptable effort is obtained. If more than one acceptable measurement is made, then the individual FRC measurements should be within 10% of each other.

Review of the raw data may be required when concerns are raised regarding test quality, and cautionary statements should be used when relevant.

Interpretation

The parameters of static lung volumes generally used in interpretation are as follows:
TLC – total lung capacity
FRC – functional residual capacity
RV – residual volume
RV/TLC – the ratio of residual volume to total lung capacity

Limits of normal

For RV and RV/TLC, generally only abnormally high results are of interest. Hence, only an upper limit of normal (ULN) is used and it is defined as +1.64 *z*-scores.

For FRC and TLC, results can be abnormally high or low. The lower limit of normal (LLN) and ULN are set at –1.96 and +1.96 *z*-scores, respectively.

Note: The current interpretation guidelines set the LLN for TLC for restriction at −1.64 *z*-scores (fifth centile) (2). It is unclear why this is the case. A possible explanation is that the basic ventilatory defect interpretation strategies only use TLC to define restriction, hence only a LLN is set. Static lung volume measurements can provide information regarding consequences of airflow limitation (e.g. hyperinflation) as well as defining restriction; therefore, it can be argued that TLC should have both ULN and LLN.

Static lung volumes are generally reported in conjunction with spirometry results because the broad classifications of ventilatory defects include parameters from both spirometry (see Chapter 2) and static lung volume measurements.

Figure 3.1 depicts a flow diagram for interpretation of ventilatory function using spirometry and TLC from static lung volume measurements.

Once spirometry and TLC have been used to determine the ventilatory pattern (Figure 3.1), other parameters from static lung volumes can assist with further defining the pattern of abnormality (Table 3.1).

Consideration of the non-specific ventilatory pattern

Defined as TLC > LLN, FEV_1/FVC > LLN, FVC and/or FEV_1 < LLN (3), the non-specific pattern, although first identified in the early 1970s (4), has received little attention in interpretation circles. The pattern has been attributed to suboptimal test performance or obstruction (primarily small airways obstruction) (2). A study published in 2011, however, found that in approximately 1200 subjects presenting with the non-specific ventilatory pattern, the pattern persisted in approximately two-thirds of individuals on follow-up. Of the remaining third, the non-specific pattern

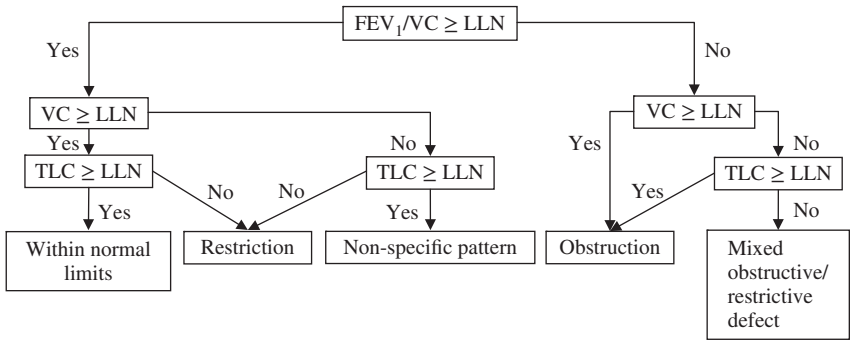


Figure 3.1 Ventilatory function interpretation strategy using spirometry and static lung volume measurements. Adapted and reproduced with permission of the European Respiratory Society: *Eur Respir J November 2005 26:948–968*; *doi:10.1183/09031936.05.00035205*.

Table 3.1 After determining the ventilatory pattern using spirometry and TLC, other parameters of static lung volumes may be used to further define the pattern of abnormality.

Using the interpretative strategy of Figure 3.1	*Parameters of static lung volumes*	*Pattern*
Within normal limits	TLC > ULN, FRC > ULN or within normal limits RV/TLC < ULN	Possible large lung size
Obstruction	TLC, FRC < ULN, RV/TLC > ULN	Gas trapping due to airflow limitation
	TLC < ULN FRC, RV/TLC > ULN	Hyperinflation (FRC)
	TLC, FRC, RV/TLC > ULN	Hyperinflation (TLC)
Restriction	TLC < LLN FRC within normal limits RV/TLC > ULN	Possible neuromuscular weakness

differentiated to obstructive patterns, restrictive patterns, mixed patterns and results in the normal range over the follow-up period (3).

Terminology

The definition of hyperinflation is contentious and is used interchangeably to describe an elevation in FRC, TLC or RV/TLC (5, 6).

In this book, gas trapping is the term used to describe an elevated RV/TLC ratio. Gas trapping occurs as a result of airflow limitation (increased resistance) and loss of elastic recoil properties of the lung (increased compliance) (7).

Hyperinflation (FRC) has been defined as an increase in the end expiratory lung volume (FRC) and a reduction in inspiratory capacity due to progressive gas trapping.

Hyperinflation (TLC) has been defined as an elevated TLC due to hyperinflation (FRC) and gas trapping (elevated RV/TLC).

Comparisons to previous results

• There are no data in the literature defining a significant change in static lung volume parameters over time, nor do interpretation guidelines mention using parameters from static lung volume measures to assess changes over time (2).

• Changes in (F)VC and FEV_1 are probably sufficient for identifying changes in ventilatory function over time.

Examples of interpretation of static lung volumes

Static lung volumes are usually interpreted in conjunction with spirometry results and interpretation is performed using the following steps as applicable:

1 Check for requirements of cautionary statements related to the following:
   a. Reference values (are values appropriate for this subject?)
   b. Quality of test (read technical comments, check raw data if required)
2 Read clinical notes
3 Follow flow chart of Figure 3.1
4 Assess spirometry loop shape
5 Assess response to inhaled bronchodilator
6 Write technical interpretation
7 Compare results to previous
8 Put results into clinical context.

Case 1

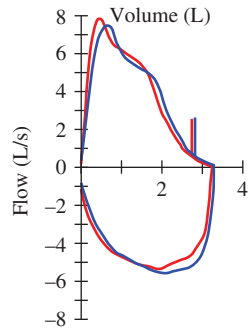
Gender:	Female		
Age (yr):	63	Weight (kg):	95
Height (cm):	162.2	Race:	Caucasian

Clinical notes: COPD, ex-smoker (20 pack years)

	Normal range	Baseline	*z*-score	Post-BD	Change (%)
Spirometry					
FEV_1 (L)	>1.88	2.74	0.79	2.83	+3
FVC (L)	>2.52	3.24	0.09	3.30	+2
FEV_1/FVC (%)	>68	85	1.20	86	
FEV_1/VC (%)	>68	81	0.53		
Static lung volumes					
TLC (L)	3.98–6.08	5.13	0.18		
RV (L)	<2.67	1.73	−0.82		
FRC (L)	1.83–3.88	2.02	−1.59		
RV/TLC (%)	<50	34	−1.20		
VC (L)	>2.52	3.40			

(*continued*)

Technical comment: Test performance was good.



Cautionary statements: The test is of good quality.
Technical interpretation: Baseline spirometry is within normal limits. The response to inhaled bronchodilator is not significant.
Static lung volumes are within normal limits.
Clinical context: Results are inconsistent with the spirometric definition of COPD. Consider alternate diagnoses.

Final report: The test is of good quality. Baseline ventilatory function is within normal limits. The response to inhaled bronchodilator is not significant. Results are inconsistent with the spirometric definition of COPD, and alternate diagnoses should be considered.
Commentary: The test is of good quality as indicated by the technical comments and VC from static lung volumes > FVC minus 150 mL (as is the case for all cases in this chapter). The clinical notes state COPD, however, the spirometric definition of COPD is the presence of obstruction on post-bronchodilator spirometry (8). This is not the case in this instance. Static lung volumes do not provide any further information towards differential diagnoses in this case. Remember that the VC from FEV_1/VC is the maximum VC obtained from spirometry or static lung volumes.

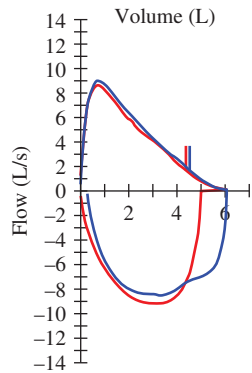
Case 2

Gender:	Male		
Age (yr):	44	Weight (kg):	87.4
Height (cm):	173.5	Race:	Caucasian

Clinical notes: Cardiomyopathy for respiratory assessment

	Normal range	Baseline	*z*-score	Post-BD	Change (%)
Spirometry					
FEV_1 (L)	>3.14	4.39	1.09	4.53	+3
FVC (L)	>4.04	6.10	2.18	6.09	+0
FEV_1/FVC (%)	>69	72	−1.19	74	
FEV_1/VC (%)	>69	72	−1.19		
Static lung volumes					
TLC (L)	5.05–8.15	8.25	2.08		
RV (L)	<2.43	2.28	1.23		
FRC (L)	1.89–4.70	4.21	1.27		
RV/TLC (%)	<35	28	0.08		
VC (L)	>4.04	5.97			

Technical comment: Test performance was good.



Cautionary statements: The test is of good quality.

Technical interpretation: Baseline spirometry is within normal limits. The response to inhaled bronchodilator is not significant.
Static lung volumes: TLC is above ULN, but RV/TLC is within the normal range. This suggests a large lung size as there is no evidence of obstruction or gas trapping.

Clinical context: No evidence of ventilatory impairment.

Final report: The test is of good quality. Baseline spirometry is within normal limits. The response to inhaled bronchodilator is not significant. Static lung volumes reveal an elevated TLC; however, RV/TLC is within normal limits suggesting a large lung size. There is no obvious ventilatory impairment.
Commentary: Some individuals have large lungs. It is important not to confuse large lung size with hyperinflation (TLC) (elevated TLC due to airflow limitation). Large lung size is likely when TLC is elevated in the presence of an RV/TLC within the normal range. Hyperinflation (TLC) is defined by an elevated TLC in the presence of an elevated RV/TLC and FRC.

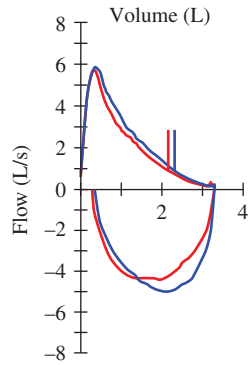
Case 3

Gender:	Female	Date:	10/1/2012
Age (yr):	53	Weight (kg):	70.5
Height (cm):	163.5	Race:	Caucasian

Clinical notes: Asthma for review

	Normal range	Baseline	*z*-score	Post-BD	Change (%)
Spirometry					
FEV_1 (L)	>2.18	2.18	−1.64	2.33	+7
FVC (L)	>2.82	3.28	−0.57	3.30	+1
FEV_1/FVC (%)	>70	66	−2.20	71	
FEV_1/VC (%)	>70	66	−2.23		
Static lung volumes					
TLC (L)	4.06–6.16	5.47	0.67		
RV (L)	<2.49	2.18	0.83		
FRC (L)	1.84–3.89	3.37	0.96		
RV/TLC (%)	<45	40	0.66		
VC (L)	>2.82	3.29			

Technical comment: Test performance was good.



Previous results:

	10/1/2012[a]	*13/12/2011*	*3/5/2011*	*15/3/2011*
FEV_1 (L)				
Baseline	2.18	2.48	2.11	
Post-BD	2.33	2.41	2.22	2.25
FVC (L)				
Baseline	3.28	3.50	3.10	
Post-BD	3.30	3.54	3.14	3.44
FEV_1/FVC (%)				
Baseline	66	71	68	
Post-BD	71	68	71	65

[a]Current result. No previous static lung volume results.

Cautionary statements: The test is of good quality.
Technical interpretation: There is an obstructive ventilatory defect with no significant response to inhaled bronchodilator. Static lung volumes are within normal limits.
Clinical context: Although there is no significant response to inhaled bronchodilator, baseline spirometry results return to within the normal range that may be of clinical significance. In comparison to previous spirometry results from 13/12/2011 and 3/5/2011, there has been no significant change.

Final report: The test is of good quality. There is an obstructive defect on baseline spirometry, with no significant response to inhaled bronchodilator, though results did return to within normal limits and may be of clinical significance. Static lung volumes are within normal limits. In comparison to previous spirometry results from 13/12/2011 and 3/5/2011, there has been no significant change.
Commentary: It is unclear why the referring doctor requested static lung volumes in this case. Nevertheless, there is obstruction on baseline spirometry that returns to within the normal range following bronchodilator although the response is not significant by definition. The question is, is this clinically important information? Static lung volumes do not add anything further to the result except that they are in the normal range.

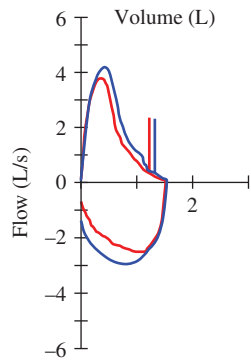
Case 4

Gender:	Female		
Age (yr):	49	Weight (kg):	93
Height (cm):	160	Race:	Caucasian

Clinical notes: Interstitial lung disease on HRCT, no previous lung function.

	Normal range	Baseline	*z*-score	Post-BD	Change (%)
Spirometry					
FEV_1 (L)	>2.17	1.25	−4.31	1.36	+9
FVC (L)	>2.77	1.54	−4.65	1.61	+5
FEV_1/FVC (%)	>71	81	0.13	84	
FEV_1/VC (%)	>71	74	−1.01		
Static lung volumes					
TLC (L)	3.85–5.95	2.81	−3.90		
RV (L)	<2.34	1.13	−1.54		
FRC (L)	1.70–3.75	1.55	−2.26		
RV/TLC (%)	<44	40	0.96		
VC (L)	>2.77	1.68			

Technical comment: Test performance was good.



Cautionary statements: The test is of good quality.
Technical interpretation: There appears to be a restrictive ventilatory defect on baseline spirometry, with no significant response to inhaled bronchodilator. Static lung volumes confirm restriction.
Clinical context: The identified restrictive defect is in keeping with interstitial lung disease.

Final report: The test is of good quality. There is a restrictive ventilatory defect. The response to inhaled bronchodilator is not significant. Results are consistent with a diagnosis of interstitial lung disease.

Commentary: In this case, spirometry and static lung volumes are used together to identify a restrictive defect.

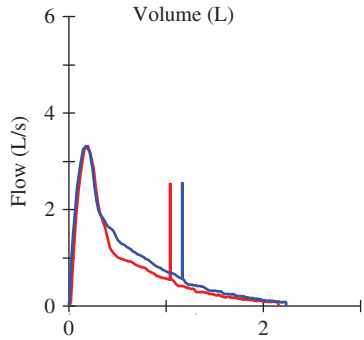
Case 5

Gender:	Male		
Age (yr):	47	Weight (kg):	102
Height (cm):	176	Race:	Caucasian

Clinical notes: Sarcoidosis

	Normal range	Baseline	*z*-score	Post-BD	Change (%)
Spirometry					
FEV_1 (L)	>3.16	1.09	−6.05	1.18	+8
FVC (L)	>4.10	2.18	−5.11	2.24	+3
FEV_1/FVC (%)	>69	50	−4.82	53	
FEV_1/VC (%)	>69	47	−5.26		
Static lung volumes					
TLC (L)	5.26–8.36	4.50	−2.92		
RV (L)	<2.55	2.20	0.71		
FRC (L)	2.03–4.85	3.03	−0.57		
RV/TLC (%)	<36	49	4.66		
VC (L)	>4.10	2.30			

Technical comment: Test performance was good.



Cautionary statements: The test is of good quality.

Technical interpretation: There is an obstructive ventilatory defect with a reduced FVC. There is no significant response to inhaled bronchodilator. The reduced TLC on static lung volumes confirms restriction and RV/TLC is elevated, suggesting gas trapping. Hence, there is a mixed obstructive/restrictive ventilatory defect.

Clinical context: Findings are consistent with sarcoidosis.

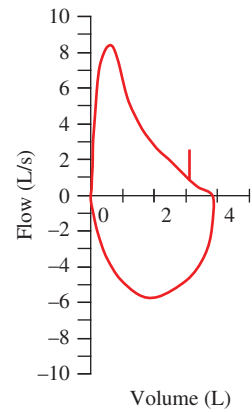
Final report: The test is of good quality. There is a mixed obstructive/restrictive ventilatory defect. The response to inhaled bronchodilator is not significant. Findings are consistent with sarcoidosis.
Commentary: A mixed obstructive and restrictive defect has been established using spirometry and static lung volume results together.
Although sarcoidosis more commonly presents as interstitial and parenchymal disease, the airways can be implicated, leading to airway obstruction also (9).

Case 6

Gender: Male
Age (yr): 47 Weight (kg): 189
Height (cm): 176 Race: Caucasian

Clinical notes: Obesity hypoventilation syndrome. ?restriction.

	Normal range	Baseline	*z*-score
Spirometry			
FEV_1 (L)	>3.16	3.10	−1.77
FVC (L)	>4.10	3.85	−2.10
FEV_1/FVC (%)	>69	81	0.37
FEV_1/VC (%)	>69	78	−0.05
Static lung volumes			
TLC (L)	5.26–8.36	5.77	−1.31
RV (L)	<2.55	1.80	−0.36
FRC (L)	2.03–4.85	1.99	−2.02
RV/TLC (%)	<36	31	0.55
VC (L)	>4.10	3.97	



Technical comment: Test performance was good.

Cautionary statements: The test is of good quality.
Technical interpretation: There appears to be a restrictive ventilatory defect on baseline spirometry, though TLC is within normal limits, suggesting a non-specific ventilatory pattern. Note that FRC is reduced in keeping with obesity.
Clinical context: The results are consistent with lung function of an individual with morbid obesity.

Final report: The test is of good quality. There is a non-specific ventilatory pattern. FRC is reduced, in keeping with morbid obesity. The results are consistent with lung function of an individual with morbid obesity.

Commentary: The combination of spirometry and static lung volumes is used to determine that there is a non-specific ventilatory pattern. Note that the FRC is reduced, with a normal TLC – this is a pattern that is often seen in morbid obesity – probably due to the weight on the chest wall leading to a lower resting end tidal volume. It is possible that the FVC is reduced also due to the inability to fully distend the chest wall due to the excess weight.

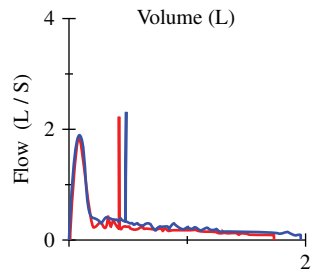
Case 7

Gender:	Male		
Age (yr):	59	Weight (kg):	54.6
Height (cm):	162.5	Race:	Caucasian

Clinical notes: COPD.

	Normal range	Baseline	*z*-score	Post-BD	Change (%)
Spirometry					
FEV_1 (L)	>2.25	0.42	−6.22	0.49	+17
FVC (L)	>3.05	1.73	−4.44	1.95	+13
FEV_1/FVC (%)	>66	24	−8.77	25	
FEV_1/VC (%)	>66	21	−9.33		
Static lung volumes					
TLC (L)	4.22–7.33	6.30	0.66		
RV (L)	<2.50	4.30	6.44		
FRC (L)	1.50–4.32	5.50	3.61		
RV/TLC (%)	<39	68	8.15		
VC (L)	>3.05	2.00			

Technical comment: Test performance was good.



(*continued*)

Cautionary statements:	The test is of good quality.
Technical interpretation:	There is an obstructive ventilatory defect with a reduced FVC on baseline spirometry. There is a significant response to inhaled bronchodilator, with incomplete reversibility of airflow limitation. Static lung volumes show hyperinflation (elevated FRC) and suggest that the reduction in FVC is due to airflow limitation.
Clinical context:	The results are consistent with COPD.

Final report: The test is of good quality. There is an obstructive ventilatory defect with evidence of hyperinflation (FRC). The response to inhaled bronchodilator is significant with incomplete reversibility of airflow limitation. The results are consistent with known COPD.
Commentary: In this case, spirometry reveals an obstructive ventilatory defect. The FVC is reduced; however, spirometry alone cannot identify the cause. Static lung volumes reveal that TLC is within normal limits, so restriction can be excluded. FRC and RV/TLC are elevated, suggesting hyperinflation (FRC) with airflow limitation, the likely cause of the reduced FVC.

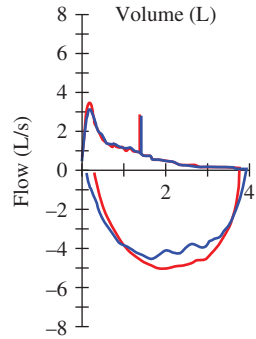
Case 8

Gender:	Male	Date:	6/2/2011
Age (yr):	50	Weight (kg):	69.6
Height (cm):	185	Race:	Caucasian

Clinical notes: COPD, smoker. For review.

	Normal range	Baseline	*z*-score	Post-BD	Change (%)
Spirometry					
FEV_1 (L)	>3.47	1.31	−5.87	1.45	+11
FVC (L)	>4.57	3.81	−2.87	3.93	+3
FEV_1/FVC (%)	>68	34	−7.37	37	
FEV_1/VC (%)	>68	31	−8.00		
Static lung volumes					
TLC (L)	6.02–9.13	9.55	2.49		
RV (L)	<2.82	5.28	8.23		
FRC (L)	2.59–5.32	6.34	3.38		
RV/TLC (%)	<37	55	5.82		
VC (L)	>4.57	4.27			

Technical comment: Test performance was good.



Previous results:

	6/2/2011[a]	*10/1/2011*
FEV_1 (L)		
Baseline	1.31	1.56
Post-BD	1.45	1.75
FVC (L)		
Baseline	3.87	3.93
Post-BD	3.93	4.13
FEV_1/FVC (%)		
Baseline	34	40
Post-BD	37	42

[a]Current result. No previous static lung volume measurements.

Cautionary statements: The test is of good quality.

Technical interpretation: There is an obstructive ventilatory defect with a reduced FVC on baseline spirometry. There is no significant response to inhaled bronchodilator. Static lung volumes show hyperinflation (elevated TLC) and suggest the reduction in FVC is due to airflow limitation.

Clinical context: There has been a significant fall in FEV_1 in comparison to spirometry results from 10/1/2011. The results are consistent with COPD.

Final report: The test is of good quality. There is an obstructive ventilatory defect with evidence of hyperinflation (TLC). The response to inhaled bronchodilator is not significant. The results are consistent with known COPD. In comparison to spirometry results from 10/1/2011, there has been a significant decline in FEV_1.

Commentary: Spirometry reveals an obstructive ventilatory defect. The FVC is reduced; however, spirometry alone cannot identify the cause. Static lung volumes reveal that TLC is elevated, so restriction can be excluded as a cause of the reduced FVC. FRC and RV/TLC are also elevated, suggesting hyperinflation (TLC) with airflow limitation, the likely cause of the reduced FVC.

References

1 Wanger J, Clausen JL, Coates A, Pedersen OF, Brusasco V, Burgos F, et al. Standardisation of the measurement of lung volumes. Eur Respir J. 2005 Sep; 26(3):511–22.

2 Pellegrino R, Viegi G, Brusasco V, Crapo RO, Burgos F, Casaburi R, et al. Interpretative strategies for lung function tests. Eur Respir J. 2005 Nov; 26(5):948–68.

3 Iyer VN, Schroeder DR, Parker KO, Hyatt RE, Scanlon PD. The nonspecific pulmonary function test: longitudinal follow-up and outcomes. Chest. 2011 Apr; 139(4):878–86.

4 Olive JT, Jr.,, Hyatt RE. Maximal expiratory flow and total respiratory resistance during induced bronchoconstriction in asthmatic subjects. Am Rev Respir Dis. 1972 Sep; 106(3):366–76.

5 Leith DE, Brown R. Human lung volumes and the mechanisms that set them. Eur Respir J. 1999 Feb; 13(2):468–72.

6 Gibson GJ. Pulmonary hyperinflation a clinical overview. Eur Respir J. 1996 Dec; 9(12):2640–9.

7 Casanova C, Cote C, de Torres JP, Aguirre-Jaime A, Marin JM, Pinto-Plata V, et al. Inspiratory-to-total lung capacity ratio predicts mortality in patients with chronic obstructive pulmonary disease. Am J Respir Crit Care Med. 2005 Mar 15; 171(6):591–7.

8 Global Strategy for the Diagnosis, Management and Prevention of COPD, Global Initiative for Chronic Obstructive Lung Disease (GOLD). 2013; Available from: http://www.goldcopd.org/ [accessed 11 March 2014].

9 Statement on sarcoidosis. Joint Statement of the American Thoracic Society (ATS), the European Respiratory Society (ERS) and the World Association of Sarcoidosis and Other Granulomatous Disorders (WASOG) adopted by the ATS Board of Directors and by the ERS Executive Committee, February 1999. Am J Respir Crit Care Med. 1999 Aug; 160(2):736–55; 10.1164/ajrccm.160.2.ats4-99; http://www.atsjournals.org/doi/pdf/10.1164/ajrccm.160.2.ats4-99 [accessed 21 March 2014].

CHAPTER 4

Carbon monoxide transfer factor: single breath method

The carbon monoxide transfer factor (T_LCO) measurement is one of the more physiologically and technically complex tests performed in the respiratory function laboratory. The T_LCO, also known as the carbon monoxide diffusing capacity (D_LCO), estimates the transfer of carbon monoxide from the alveolar gas to the red blood cell and represents the integrity of the gas exchange process of the alveolar–capillary membrane. The most commonly used method to measure the T_LCO is the single breath method, which is discussed in this chapter.

The test is performed by asking the subject to attach to a mouthpiece and commence tidal breathing with lips tightly sealed and a nose peg in place. After a couple of tidal breaths, the subject is asked to exhale to residual volume (RV) and then take a rapid vital capacity (VC) breath in of a special test gas mixture to total lung capacity (TLC). The test gas mixture consists of carbon monoxide (CO), oxygen and nitrogen and an inert gas, commonly helium or methane. Once at TLC, the subject breath holds for approximately 8 s and then exhales to RV again. The first portion of the exhaled breath is discarded (dead space washout) and a sample of the remaining exhaled breath is collected for analysis (Figure 4.1). From the gas analysis, volume measurements and timing, parameters of carbon monoxide transfer factor can be calculated. A detailed explanation of the test methodology and calculations can be found in (1).

The parameters of carbon monoxide transfer factor used in the assessment of test quality and interpretation are as follows:

- T_LCO: The transfer of CO across the lung; a measure of the ease of transfer of gas across the lung.
  - Units: mmol/min/kPa (SI units) or mL/min/mmHg.

Interpreting Lung Function Tests: A Step-by-Step Guide, First Edition.
Brigitte M. Borg, Bruce R. Thompson and Robyn E. O'Hehir.
© 2014 John Wiley & Sons, Ltd. Published 2014 by John Wiley & Sons, Ltd.

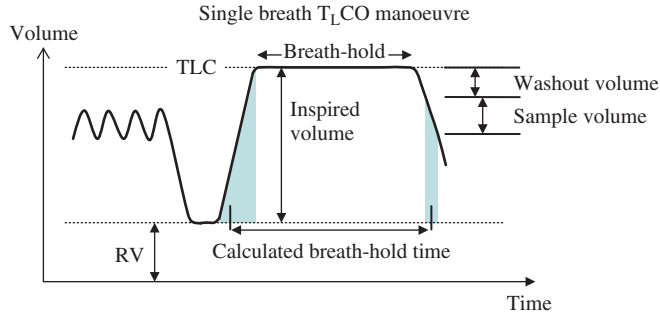


Figure 4.1 Spirogram of the single breath carbon monoxide transfer factor manoeuvre.

— To convert mmol/min/kPa to mL/min/mmHg, multiply T_LCO by 2.987.

- V_A, alveolar volume: the alveolar volume participating in gas exchange.
  — Units: litres (L)
- KCO, transfer coefficient: the efficiency of uptake of CO in the alveoli, kCO, corrected for barometric pressure in the lung.
  — Units: mmol/min/kPa/L (SI units) or mL/min/mmHg/L
- V_I, the inspired volume: used for quality assessment.
  — Units: L
- T_LCO_{Hbcorr}: the T_LCO corrected to a standard haemoglobin value (described in more detail later).

Test quality

- Acceptability criteria (1):
  — V_I is ≥85% of the largest VC.
  — V_I occurs in less than 4 s.
  — Breath-hold time is 10 ± 2 s.
  — Breath hold is stable with no evidence of Mueller or Valsalva manoeuvres, or leaks.
  — Expiration of washout and sample collection occurs in <4 s (<3 s for sample collection time).
  — Appropriate clearance of dead space volume.
  — Proper analysis of alveolar gas sample.
- Repeatability criteria(1):
  — A minimum of two acceptable tests.
  — The values of each test are within 1 mmol/min/kPa or within 10% of the highest value.
- Tests not meeting the above criteria must be interpreted with caution.

— Breath hold and sample collection times are often increased in obstruction.

— $V_I < 85\%$ of largest VC: T_LCO and VA may be reduced when there is a failure to inhale to TLC. If V_I is reduced due to an inability to exhale to RV, but a breath to TLC is achieved, there is thought to be little effect on T_LCO or V_A.

— Increasing or decreasing pulmonary capillary blood volume may lead to overestimation or underestimation of T_LCO, respectively.

— Inadequate washout of dead space prior to collecting sample may lead to underestimation of T_LCO.

— Where leaks are detected – the effort should be rejected and not used for interpretation.

- Test quality should be noted by the operator in the technical comment to inform those interpreting results.

Factors to consider during interpretation

The carbon monoxide transfer factor test makes an assessment of gas exchange. Therefore, apart from the technical factors involved in the performance of the test, other factors that may impact on gas exchange need to be taken into consideration during interpretation.

Carbon monoxide transfer factor (T_LCO)

T_LCO may be affected by factors as shown in Table 4.1. Some of these factors can be accounted for by strict adherence to test performance criteria or by applying corrections to the measured values.

The effects of some of these factors are described in more detail:

- Haemoglobin (Hb)

  — A reduced Hb results in a lower T_LCO, and an increased Hb results in a higher T_LCO due to the reduced or increased binding sites for CO on red blood cells, respectively.

  — T_LCO values are often standardised to account for variability of haemoglobin. The parameter is notated as T_LCO_{Hbcorr} (T_LCO corrected for Hb) and is standardised to Hb of 13.4 g/dL for children (<15 years) and females, and 14.6 g/dL for males. Haemoglobin correction equations are available in (1).

  — Both the T_LCO corrected and uncorrected for haemoglobin are important to consider in interpretation. The T_LCO_{Hbcorr} provides insight into the integrity of the alveolar membrane and pulmonary vasculature, allowing comparisons to be made over time without the complication of variation in haemoglobin. The uncorrected T_LCO

Table 4.1 Factors affecting $T_L CO$.

$T_L CO$ may be reduced due to following reasons:	*Examples:*
• Reduction in the alveolar membrane surface area.	• Emphysema, incomplete alveolar expansion, loss of lung units
• Increased thickness of the alveolar membrane	• Disorders of the interstitium, pulmonary oedema
• Reduction in pulmonary capillary blood volume	• Pulmonary embolus, pulmonary hypertension, microvascular destruction, Valsalva manoeuvre
• Anaemia	• Reduced haemoglobin, elevated carboxyhaemoglobin
• Changes in gas composition in the lung	• Increased P_IO_2 due to supplemental oxygen
$T_L CO$ may be increased due to following reasons:	
• Changes in gas composition in the lung	• Low P_IO_2 due to altitude, increased P_ACO_2
• Increases in pulmonary capillary blood volume	• Exercise, redistribution of blood flow due to pneumonectomy, Mueller manoeuvre
• Polycythaemia	• Sometimes seen as a result of impaired gas exchange
• Blood in alveolar spaces	• Pulmonary haemorrhage
• Posture	• Supine posture

provides information about functionality. For example, Case 5 shows that the integrity of the alveolar membrane and pulmonary vasculature is intact ($T_L CO_{corrHb} > LLN$), while the uncorrected $T_L CO$ shows impaired gas exchange, due to anaemia, impacting on the subject's functionality.

- Carboxyhaemoglobin (COHb)
  — An elevated COHb results in an underestimation of $T_L CO$ due to a decreased diffusion gradient of CO from the alveolus to capillary blood, and due to the creation of an anaemia-like effect due to reduced binding sites.
  — Smoking and exposure to cigarettes and other environmental sources may produce sufficient levels of CO to adversely affect $T_L CO$ measurement. Carbon monoxide correction equations are available in (1).
  — Where a correction for COHb is not made, a cautionary comment could be added to the report describing the possible increased exposures (for example, cigarette smoking prior to test – 5 in last 4 h – may result in underestimation of $T_L CO$).

- Alveolar pO_2

  — An increased P_AO_2, for example, seen in patients on supplemental oxygen therapy, results in an underestimated T_LCO due to increased competition for CO to haemoglobin-binding sites. Similarly, hyperventilation can also affect P_AO_2 and T_LCO.

    - Subjects on supplemental oxygen should have oxygen therapy removed for at least 10 min prior to the test being performed, where it is safe to do so, to minimise this effect. Correction equations for tests performed at higher P_AO_2 are available in (1).

  — A decreased P_AO_2, as a result of assessment at altitude, for example, results in an overestimated T_LCO due to reduced competition for CO to haemoglobin-binding sites. Correction equations for tests performed at altitude are available in (1). P_AO_2 can also be reduced as a result of an increased P_ACO_2. It has been estimated that for every 0.133 kPa fall in P_AO_2, T_LCO will increase by 0.31–0.35% (1).
- Pulmonary capillary blood volume.

  — Increases in pulmonary capillary blood volume will result in increases in T_LCO (e.g. Mueller manoeuvre, exercise) and decreases in blood volume will result in falls in T_LCO (e.g. Valsalva manoeuvre). Avoidance of these conditions is included as acceptability criteria for the test.

  — Moving from an upright to supine posture will result in an increase in T_LCO due to changes in the distribution of the blood volume throughout the lung.

  — There is some suggestion that changes in blood volume/distribution in the lungs account for increases in T_LCO seen in some subjects with stable asthma or obesity (2).

Alveolar volume

V_A may be reduced due to the following reasons:

- Incomplete expansion of the lungs (e.g. neuromuscular disease, incomplete inhalation to TLC)
- Loss of lung units (e.g. pneumonectomy, atelectasis, localised lung destruction)
- Poor mixing of inspired gas (e.g. significant airflow obstruction)

In an individual, it is possible that a reduced V_A may be the result of more than one of the above causes (2).

The transfer coefficient, KCO

KCO will be affected by conditions affecting T_LCO or V_A.

Interpretation

- The main parameters used for the interpretation of T_LCO are as follows:
  - T_LCO
  - V_A
  - KCO

Carbon monoxide transfer factor test results are generally reported in conjunction with spirometry. Static lung volumes (SLV), TLC in particular, can also be helpful in interpreting changes in V_A (*see later*).

Limits of the normal range

1 For T_LCO and V_A, generally abnormally low results are of interest. The LLN is set at a *z*-score of −1.64.
2 For KCO, both abnormally high and low results are of interest. The upper limit for normal (ULN) and lower limit of normal (LLN) are set at *z*-scores of ±1.96.

A reduced T_LCO is functionally abnormal regardless of the cause (e.g. anaemia, reduced V_A, parenchymal dysfunction).
- The impact of haemoglobin and carboxyhaemoglobin on T_LCO should be considered where information is available. T_LCO may be reduced due to transport issues primarily (anaemia, CO back pressure) rather than parenchymal or pulmonary vascular abnormalities.
- Similarly, the impact of changes in P_IO_2 should be accounted for where required.

Corrections for haemoglobin and carboxyhaemoglobin

Be consistent with the parameters used for reporting of T_LCO.

Articulate clearly in reports whether the T_LCO parameter being commented on has had any corrections for haemoglobin and/or carboxyhaemoglobin applied.

For example, T_LCO corrected for haemoglobin might be reported as follows:

> *Carbon monoxide transfer factor, corrected for haemoglobin, is …*

or T_LCO corrected for haemoglobin and carboxyhaemoglobin:

> *Carbon monoxide transfer factor, corrected for haemoglobin and carboxyhaemoglobin, is …*

or, T_LCO without corrections, then

> *Carbon monoxide transfer factor, uncorrected for haemoglobin, is …*

When V_A is reduced, TLC measured by SLV (plethysmography or multiple breath washout) may provide information regarding the cause:

- There is a relationship between worsening airway obstruction (FEV_1/FVC) and a worsening V_A/TLC (3, 4), probably explained by poor gas mixing.
- A V_A/TLC close to unity may indicate loss of lung units as the cause of a reduced V_A (3, 4).

Table 4.2 offers a strategy for interpretation using T_LCO, V_A and KCO.

KCO in the interpretation strategy

At the time of writing, the value of KCO in the interpretation strategy is uncertain and controversial. Although some (2) stress that KCO plays an integral role in the assessment of gas exchange and utilise it as a primary parameter in the interpretation strategy, others (5, 6) remain cautious about its value in the interpretation strategy and believe it has little role in interpretation of gas exchange.

Part of the reason for the differing views may be that KCO is often incorrectly described as a 'correction for alveolar volume'. KCO is a rate constant describing the carbon monoxide transfer factor per unit alveolar volume for the alveolar volume at which the measurement is made. The

Table 4.2 Interpretation strategy for carbon monoxide transfer factor using T_LCO, V_A and KCO.

T_LCO	*Other parameters*	*Report*
>LLN	V_A > LLN	T_LCO is within normal limits
	V_A < LLN	T_LCO is within normal limits in the presence of a reduced alveolar volume
<LLN	V_A > LLN	Alveolar volume is within normal limits and T_LCO is reduced, suggestive of parenchymal or pulmonary vascular disease
	V_A < LLN KCO < LLN	Both T_LCO and V_A are reduced with a decreased KCO, suggestive of parenchymal or pulmonary vascular disease
	V_A < LLN LLN < KCO < ULN	Both T_LCO and V_A are reduced. As the KCO is in the normal range, the T_LCO may be reduced due to the reduction in alveolar volume, parenchymal or pulmonary vascular disease or a combination of these.
	V_A < LLN KCO > ULN	Both T_LCO and V_A are reduced. The elevated KCO suggests that the reduction in T_LCO is due to incomplete expansion of alveoli rather than parenchymal or pulmonary vascular disease.

relationship between T_LCO and V_A, measured as a proportion of TLC, is not linear (i.e. KCO changes as V_A/TLC changes) (2) and, therefore, cannot be described as 'correction'. For a detailed review of the use of KCO in interpretation, see (2).

For simplicity, we have used KCO in the interpretation strategy only after T_LCO and V_A have been examined. This limits the role of the KCO to a few isolated situations as follows:

1 When both T_LCO and V_A are reduced and:
- — KCO is elevated (>ULN), factors external to the lungs should be considered as the cause. KCO tends to be elevated when there is incomplete expansion of alveoli to TLC (e.g. poor inspiratory effort, respiratory muscle weakness, chest wall restriction) (2, 5).
- — KCO is in the normal range, interpret with caution. Pathology may be present when KCO is normal in the presence of a reduced T_LCO and V_A. The result may be due to loss of lung units (discrete or diffuse), poor gas mixing, parenchymal or pulmonary vascular dysfunction or a combination of these. (2)
- — KCO is low (<LLN), parenchymal or pulmonary vascular disease is probably the predominant cause (2, 7).

2 When T_LCO is in the normal range and V_A is reduced:
- — Where KCO is elevated (>ULN), consider
  - incomplete alveolar expansion (see explanation earlier).

3 When T_LCO is in the normal range (usually markedly increased) and V_A is within normal limits or reduced:
- — Where KCO is elevated (>ULN), consider
  - alveolar haemorrhage (2).

Comparison to previous results

- Published studies (8, 9) suggest that a change > ±1.60 mmol/min/kPa over the short term and >10% in the longer term (year) probably reflect clinically significant changes.

Examples of interpretation of carbon monoxide transfer factor

Interpretation is performed using the following steps as applicable:

1 Check for requirements of cautionary statements related to the following:

a. Reference values (are values appropriate for this subject? See Chapter 1 for details.).

b. Quality of test (read technical comments, check raw data if required).

c. Factors affecting T_LCO measurement (e.g. noting recent smoking if no correction for COHb is made).

2 Read clinical notes
3 Interpret spirometry
4 Interpret SLV measurements (if available)
5 Assess response to inhaled bronchodilator (BD)
6 Assess spirometry loop shape
7 Interpret T_LCO (Table 4.2)
8 Write technical interpretation
9 Compare results to previous
10 Put results into clinical context

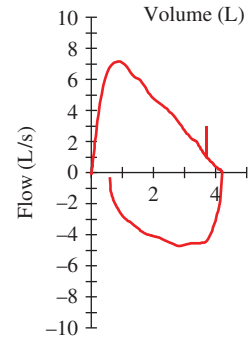
In the following examples, corrections have been made for haemoglobin. No corrections for altitude have been made as tests were performed near sea level. No corrections for carboxyhaemoglobin are required and no corrections for increased P_IO_2 (supplemental oxygen) are required.

Case 1

Gender:	Female		
Age (yr):	28	Weight (kg):	69
Height (cm):	170	Race:	Caucasian

Clinical notes: Exposure to laser smoke

	Normal range	Baseline	*z*-score
Spirometry			
FEV_1 (L)	>2.86	3.73	+0.59
FVC (L)	>3.39	4.22	+0.15
FEV_1/FVC (%)	>75	88	+0.59
FEV_1/VC (%)	>75	88	+0.59
Static lung volumes			
TLC (L)	4.44–6.54	5.72	+0.42
RV (L)	<2.12	1.69	+0.52
FRC (L)	2.00–4.05	3.25	+0.43
RV/TLC (%)	<35	30	+0.73
VC (L)	>3.39	4.03	
Single breath carbon monoxide transfer factor			
V_I (L)		3.83	
V_A (L)	>4.4	5.7	+0.23
T_LCO (mmol/min/kPa)	>6.6	10.0	+0.87
$T_LCO_{Hb\ corr}$ (mmol/min/kPa)		9.9	+0.85
KCO (mmol/min/kPa/L)	1.1–2.1	1.7	+0.52
$KCO_{Hb\ corr}$ (mmol/min/kPa/L)		1.7	+0.50
Hb (g/dL)		13.5	



Technical comment: Test performance was good.

Cautionary statements: The test is of good quality.

Technical interpretation: Baseline spirometry is within normal limits. SLV are within normal limits. Alveolar volume and carbon monoxide transfer factor, corrected for haemoglobin, are within normal limits.

Clinical context: Lung function is within normal limits. No evidence of an abnormality detected on this occasion.

Final report: The test is of good quality. Baseline ventilatory function is within normal limits. Carbon monoxide transfer factor, corrected for haemoglobin, is within normal limits. No evidence of an abnormality detected on this occasion.

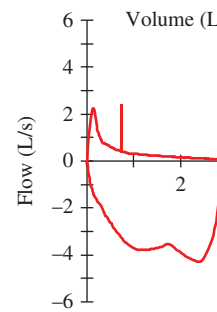
Commentary: This case provides an example of results that are within normal limits.

Case 2

Gender:	Female		
Age (yr):	51	Weight (kg):	51
Height (cm):	161	Race:	Caucasian

Clinical notes: COPD, emphysema on HRCT.

	Normal range	Post-BD	*z*-score
Spirometry			
FEV_1 (L)	>2.15	0.76	−5.63
FVC (L)	>2.77	2.90	−1.32
FEV_1/FVC (%)	>70	26	−9.03
FEV_1/VC (%)	>70	22	−9.73
Static lung volumes			
TLC (L)	3.91–6.01	5.80	+1.56
RV (L)	<2.40	2.35	+1.51
FRC (L)	1.75–3.80	3.59	+1.56
RV/TLC (%)	<45	41	+1.00
VC (L)	>2.77	3.45	
Single breath carbon monoxide transfer factor			
V_I (L)		2.80	
V_A (L)	>4.1	4.2	−1.48
T_LCO (mmol/min/kPa)	>5.4	2.1	−5.20
$T_LCO_{Hb\ corr}$ (mmol/min/kPa)		2.1	−5.24
KCO (mmol/min/kPa/L)	1.0–1.8	0.5	−4.32
$KCO_{Hb\ corr}$ (mmol/min/kPa/L)		0.5	−4.35
Hb (g/dL)		14.2	



Technical comment: Test performance was good.

Cautionary statements: The test is of good quality.

Technical interpretation: There is an obstructive ventilatory defect on post-bronchodilator spirometry. SLV are within normal limits. Alveolar volume is within normal limits and carbon monoxide transfer factor, corrected for haemoglobin, is reduced, suggestive of parenchymal or pulmonary vascular disease.

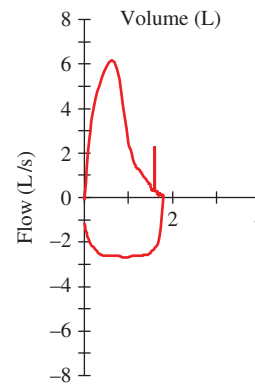
Clinical context: Results are consistent with a diagnosis of emphysema.

Final report: The test is of good quality. There is an obstructive defect on post-bronchodilator ventilatory function. Alveolar volume is within normal limits and carbon monoxide transfer factor, corrected for haemoglobin, is reduced, suggestive of parenchymal or pulmonary vascular disease. Results are consistent with a diagnosis of emphysema.
Commentary: Obstruction on post-bronchodilator spirometry is consistent with the spirometric definition of COPD (see Chapter 2). The reduced T_LCO suggests gas exchange impairment. These findings are consistent with the HRCT findings of emphysema.

Case 3

Gender:	Female		
Age (yr):	33	Weight (kg):	178
Height (cm):	165	Race:	Caucasian
Clinical notes:	Obesity hypoventilation syndrome		

	Normal range	Baseline	*z*-score
Spirometry			
FEV_1 (L)	>2.63	1.62	−4.40
FVC (L)	>3.17	1.80	−4.80
FEV_1/FVC (%)	>74	90	+1.04
FEV_1/VC (%)	>74	77	−1.18
Static lung volumes			
TLC (L)	4.15–6.25	2.90	−4.29
RV (L)	<2.12	0.89	−1.58
FRC (L)	1.84–3.89	1.04	−3.48
RV/TLC (%)	<37	31	+0.54
VC (L)	>3.17	2.11	
Single breath carbon monoxide transfer factor			
V_I (L)		1.99	
V_A (L)	>4.1	2.6	−3.91
T_LCO (mmol/min/kPa)	>6.2	6.0	−1.77
$T_LCO_{Hb\ corr}$ (mmol/min/kPa)		5.6	−2.08
KCO (mmol/min/kPa/L)	1.1–2.1	2.3	+2.60
$KCO_{Hb\ corr}$ (mmol/min/kPa/L)		2.2	+2.10
Hb (g/dL)		16.1	



Technical comment: Test performance was good.

Cautionary statements:	The test is of good quality.
Technical interpretation:	BMI is 65 kg/m^2. There appears to be a restrictive ventilatory defect on spirometry, which is confirmed by SLV. Both T_LCO, corrected for haemoglobin, and VA are reduced. The elevated KCO suggests that the reduction in T_LCO is due to incomplete expansion of alveoli rather than parenchymal or pulmonary vascular disease. Note: Hb 16.1 g/dL.
Clinical context:	Results appear to be in keeping with pattern seen with morbid obesity.

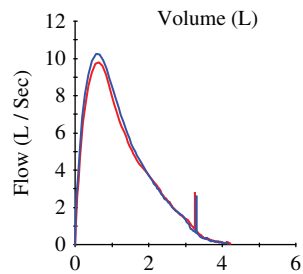
Final report: The test is of good quality. There is a restrictive ventilatory defect. Both alveolar volume and carbon monoxide transfer factor, corrected for haemoglobin, are reduced. Results suggest that the reduction in T_LCO is due to incomplete expansion of alveoli rather than parenchymal or pulmonary vascular disease. These results are in keeping with the pattern seen with morbid obesity.
Commentary: This case illustrates a reduced T_LCO due to factors external to the lung causing incomplete expansion of alveoli (KCO *z*-score $>$ 1.96). In this case, the excess weight on the chest may be preventing complete expansion of the chest wall or the inability to displace the diaphragm due to abdominal weight may be preventing completed expansion of the lungs. Note that FRC is reduced in keeping with obesity (FRC is close to RV); the patient tidal breathes at a lower volume to reduce work of breathing.

Case 4

Gender:	Male		
Age (yr):	67	Weight (kg):	67.8
Height (cm):	169.5	Race:	Caucasian
Clinical notes:	Congestive cardiac failure		

	Normal range	Baseline	*z*-score	Post-BD	Change (%)
Spirometry					
FEV_1 (L)	>2.24	3.27	+0.72	3.32	+2
FVC (L)	>3.15	4.22	+0.43	4.15	−2
FEV_1/FVC (%)	>65	77	+0.55	80	
FEV_1/VC (%)	>65	74	−0.04		
Static lung volumes					
TLC (L)	4.80–7.91	6.84	+0.61		
RV (L)	<2.82	2.42	+0.57		
FRC (L)	1.91–4.72	3.56	+0.34		
RV/TLC (%)	<42	35	+0.05		
VC (L)	>3.15	4.42			
Single breath carbon monoxide transfer factor					
V_I (L)		4.03			
V_A (L)	>5.2	6.3	+0.03		
T_LCO (mmol/min/kPa)	>6.2	5.7	−2.12		
$T_LCO_{Hb\ corr}$ (mmol/min/kPa)		5.9	−1.96		
KCO (mmol/min/kPa/L)	0.9–1.6	0.9	−2.28		
$KCO_{Hb\ corr}$ (mmol/min/kPa/L)		0.9	−2.08		
Hb (g/dL)		13.4			

Technical comment: Test performance was good.



Cautionary statements:	The test is of good quality.
Technical interpretation:	Baseline spirometry is within normal limits. There is no significant response to inhaled bronchodilator. SLV are within normal limits. Alveolar volume is within normal limits and carbon monoxide transfer factor, corrected for haemoglobin, is reduced. Results suggest parenchymal or pulmonary vascular disease.
Clinical context:	Results are consistent with the pattern seen in congestive cardiac failure.

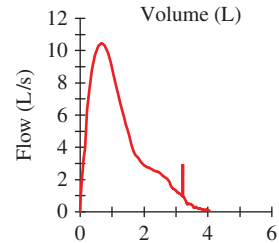
Final report: The test is of good quality. Baseline ventilatory function is within normal limits. There is no significant response to inhaled bronchodilator. Alveolar volume is within normal limits and carbon monoxide transfer factor, corrected for haemoglobin, is reduced, suggestive of parenchymal or pulmonary vascular disease. Results are consistent with the pattern seen in congestive cardiac failure. *Commentary*: Although lung function is not diagnostic of congestive heart failure, a reduced T_LCO in the presence of normal spirometry or a restricted ventilatory defect is consistent with the pattern seen in patients with congestive cardiac failure. The T_LCO may be reduced as a function of poor cardiac output, changes in pulmonary artery pressure and/or pulmonary oedema.

Case 5

Gender:	Male		
Age (yr):	61	Weight (kg):	84
Height (cm):	178	Race:	Caucasian

Clinical notes: ?asthma. Cough, SOB. For bronchial provocation test.

	Normal range	Baseline	*z*-score
Spirometry			
FEV_1 (L)	>2.80	3.24	−0.72
FVC (L)	>3.82	4.10	−1.15
FEV_1/FVC (%)	>66	79	+0.61
FEV_1/VC (%)	>66	78	+0.51
Static lung volumes			
TLC (L)	5.46–8.57	6.52	−0.62
RV (L)	<2.88	2.39	+0.33
FRC (L)	2.25–5.07	3.56	−0.14
RV/TLC (%)	<40	37	+0.93
VC (L)	>3.82	4.13	
Single breath carbon monoxide transfer factor			
V_I (L)		3.83	
V_A (L)	>5.9	6.3	−1.02
$T_L CO$ (mmol/min/kPa)	>7.4	6.1	−2.71
$T_L CO_{Hb\ corr}$ (mmol/min/kPa)		10.6	+0.93
KCO (mmol/min/kPa/L)	1.0–1.7	1.0	−2.23
$KCO_{Hb\ corr}$ (mmol/min/kPa/L)		1.7	+2.07
Hb (g/dL)		5.2	



Technical comment: Test performance was good. Challenge test booked but not performed due to finding of anaemia. After consultation with referring physician, subject referred to emergency department for investigation and treatment of anaemia. Hb from full blood examination.

Cautionary statements:	The test is of good quality. Challenge test booked but not performed due to finding of anaemia. After consultation with referring physician, subject taken to emergency department for investigation of anaemia.
Technical interpretation:	Baseline spirometry is within normal limits. SLV are within normal limits. Alveolar volume and carbon monoxide transfer factor, corrected for haemoglobin, are within normal limits. Note: Hb 5.2 g/dL, hence the uncorrected carbon monoxide transfer factor, is reduced due to anaemia.
Clinical context:	The uncorrected carbon monoxide transfer factor is reduced due to anaemia.

Final report: The test is of good quality. Baseline ventilatory function is within normal limits. Alveolar volume and carbon monoxide transfer factor, corrected for haemoglobin, are within normal limits. Note: Haemoglobin is 5.2 g/dL, resulting in a reduced uncorrected carbon monoxide transfer factor. Bronchial provocation test was not performed on this occasion due to the finding of anaemia, but can be re-booked if clinically indicated in the future. The patient was referred to the emergency department for investigation and treatment of anaemia following the assessment.

Commentary: This case highlights the importance of measuring Hb to adjust the measured T_LCO. The uncorrected T_LCO is below the LLN and after correcting for Hb, the T_LCO returns to within normal limits (in this case, the Hb correction increases the T_LCO by 4.5 units). Without the haemoglobin corrected T_LCO, it is unclear if the TLCO is reduced because of the following conditions:

1 There is a functional issue with the ability of the blood to carry carbon monoxide (and hence oxygen)

2 There is a problem with the alveolar capillary membrane itself, or

3 A combination of both 1 and 2?

Having both haemoglobin corrected and uncorrected T_LCO values provides clarity that the reduced T_LCO is due to anaemia and the alveolar capillary membrane appears to be functioning normally.

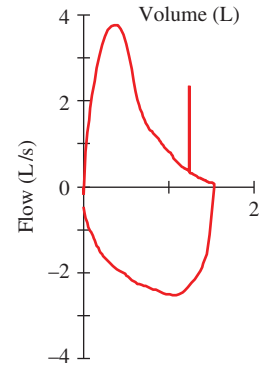
Case 6

Gender:	Female		
Age (yr):	49	Weight (kg):	70
Height (cm):	160	Race:	Caucasian

Clinical notes: Interstitial lung disease.

	Normal range	Baseline	*z*-score
Spirometry			
FEV_1 (L)	>2.17	1.25	−4.31
FVC (L)	>2.77	1.54	−4.65
FEV_1/FVC (%)	>71	81	+0.13
FEV_1/VC (%)	>71	74	−1.01
Static lung volumes			
TLC (L)	3.85–5.95	2.81	−3.90
RV (L)	<2.34	1.13	−1.54
FRC (L)	1.70–3.75	1.55	−2.26
RV/TLC (%)	<44	40	+0.96
VC (L)	>2.77	1.68	
Single breath carbon monoxide transfer factor			
V_I (L)		1.54	
V_A (L)	>4.0	2.3	−4.66
T_LCO (mmol/min/kPa)	>5.7	2.1	−5.54
$T_LCO_{Hb\ corr}$ (mmol/min/kPa)		2.1	−5.54
KCO (mmol/min/kPa/L)	1.1–1.9	0.9	−2.77
$KCO_{Hb\ corr}$ (mmol/min/kPa/L)		0.9	−2.77
Hb (g/dL)		13.5	

Technical comment: Test performance was good.



Cautionary statements: The test is of good quality.

Technical interpretation: There appears to be a restrictive defect on spirometry. This is confirmed by a reduced TLC on SLV. Both alveolar volume and carbon monoxide transfer factor, corrected for haemoglobin, are reduced. KCO is also reduced, suggesting parenchymal or pulmonary vascular disease.

Clinical context: These results are in keeping with interstitial lung disease.

Final report: The test is of good quality. There is a restrictive ventilatory defect. Both alveolar volume and carbon monoxide transfer factor, corrected for haemoglobin, are reduced. The transfer coefficient is also reduced, suggesting parenchymal or

pulmonary vascular disease. These findings are consistent with a diagnosis of interstitial lung disease.

Commentary: Although lung function testing is not able to specifically diagnose interstitial lung disease, established interstitial lung disease commonly presents as a restrictive ventilatory defect with gas exchange impairment. In early disease, gas exchange impairment with no evidence of restriction may be seen. This case is an example of the typical pattern seen with interstitial lung disease.

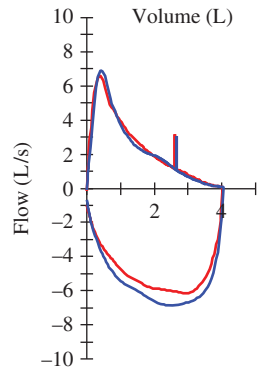
Case 7

Gender:	Male		
Age (yr):	42	Weight (kg):	86
Height (cm):	167.5	Race:	Caucasian

Clinical notes: ?asthma, ?COPD

	Normal range	Baseline	*z*-score	Post-BD	Change (%)
Spirometry					
FEV_1 (L)	>2.96	2.62	−2.44	2.67	+2
FVC (L)	>3.76	4.09	−0.99	4.05	−1
FEV_1/FVC (%)	>70	64	−2.61	66	
FEV_1/VC (%)	>70	63	−2.71		
Single breath carbon monoxide transfer factor					
V_I (L)		4.13			
V_A (L)	>4.7	7.3	+1.52		
T_LCO (mmol/min/kPa)	>7.7	10.8	+0.30		
$T_LCO_{Hb\ corr}$ (mmol/min/kPa)		11.4	+0.67		
KCO (mmol/min/kPa/L)	1.2–2.2	1.5	−0.87		
$KCO_{Hb\ corr}$ (mmol/min/kPa/L)		1.6	−0.45		
Hb (g/dL)		12.9			

Technical comment: Test performance was good.



(*continued*)

Cautionary statements:	The test is of good quality.
Technical interpretation:	There is an obstructive ventilatory defect. There is no significant response to inhaled bronchodilator. Carbon monoxide transfer factor, corrected for haemoglobin, is within normal limits, as is alveolar volume.
Clinical context:	Results are consistent with the spirometric definition of COPD but asthma with fixed airflow limitation cannot be excluded. Gas exchange appears to be intact.

Final report: The test is of good quality. There is an obstructive ventilatory defect with no significant response to inhaled bronchodilator. Carbon monoxide transfer factor, corrected for haemoglobin, is within normal limits. Results are consistent with the spirometric definition of COPD, but asthma with fixed airflow limitation cannot be excluded. Gas exchange appears to be intact, suggesting emphysema (unless early disease) is unlikely. Clinical correlation is required.

Commentary: COPD is defined spirometrically by obstruction on post-bronchodilator spirometry. These results fit this definition. Spirometry cannot differentiate between asthma and fixed airflow limitation, emphysema, chronic bronchitis, bronchiectasis or other pathologies that result in fixed airflow limitation. Measurement of gas exchange may reduce the number of differential diagnoses as gas exchange impairment is a feature of some obstructive lung diseases, but not others. In this case, T_LCO suggests that the gas exchange regions of the lungs are unaffected. Hence, obstructive diseases with gas exchange impairment (e.g. emphysema) are less likely though cannot be ruled out completely (the development of high-resolution computed tomography has resulted in emphysema being identified via imaging before it is identified via lung function tests). Some studies suggest T_LCO may be increased in subjects with asthma (2). In this case, the T_LCO is within the normal range so does not assist with differentiating further. Measurement of T_LCO to differentiate between COPD and asthma in this particular case has not been helpful.

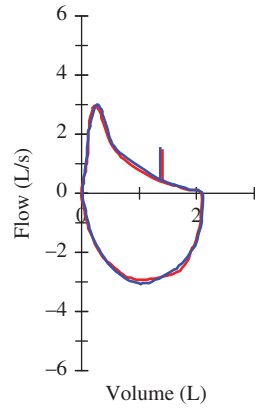
Case 8

Gender:	Female		
Age (yr):	65	Weight (kg):	80
Height (cm):	166.4	Race:	Caucasian

Clinical notes: Ex-smoker (40 pack years), on amiodarone.

	Normal range	Baseline	*z*-score	Post-BD	Change (%)
Spirometry					
FEV_1 (L)	>1.95	1.34	−3.28	1.40	+4
FVC (L)	>2.62	2.11	−2.81	2.09	−1
FEV_1/FVC (%)	>67	64	−2.27	67	
FEV_1/VC (%)	>67	64	−2.27		
Static lung volumes					
TLC (L)	4.23–6.33	4.51	−1.44		
RV (L)	<2.79	2.42	+0.67		
FRC (L)	1.98–4.03	2.84	−0.32		
RV/TLC (%)	<50	54	+2.31		
VC (L)	>2.62	2.11			
Single breath carbon monoxide transfer factor					
V_I (L)		2.05			
V_A (L)	>4.2	3.7	−2.52		
T_LCO (mmol/min/kPa)	>5.0	4.8	−1.87		
$T_LCO_{Hb\ corr}$ (mmol/min/kPa)		4.9	−1.76		
KCO (mmol/min/kPa/L)	0.9–1.7	1.3	+0.16		
$KCO_{Hb\ corr}$ (mmol/min/kPa/L)		1.4	+0.33		
Hb (g/dL)		12.7			

Technical comment: Test performance was good.



(*continued*)

Cautionary statements:	The test is of good quality.
Technical interpretation:	There is an obstructive ventilatory defect with a reduced FVC. There is no significant response to inhaled bronchodilator. The FVC is likely to be reduced due to gas trapping/airflow limitation (TLC is within normal limits, RV/TLC is elevated). Both alveolar volume and carbon monoxide transfer factor, corrected for haemoglobin, are reduced. As the KCO is in the normal range, the T_LCO may be reduced due to the reduction in alveolar volume, parenchymal or pulmonary vascular disease or a combination of these.
Clinical context:	Results are consistent with the spirometric definition of COPD, and there is evidence of gas exchange impairment that could be due to emphysema or associated with early interstitial disease due to amiodarone. Clinical correlation is required.

Final report: The test is of good quality. There is an obstructive ventilatory defect with no significant response to inhaled bronchodilator. SLV suggest gas trapping. Both alveolar volume and carbon monoxide transfer factor, corrected for haemoglobin, are reduced. Results suggest that the T_LCO may be reduced due to the reduction in alveolar volume, parenchymal or pulmonary vascular disease or a combination of these. Results are consistent with the spirometric definition of COPD. There is evidence of gas exchange impairment that could be associated with emphysema or early interstitial disease due to amiodarone. Clinical correlation is required.

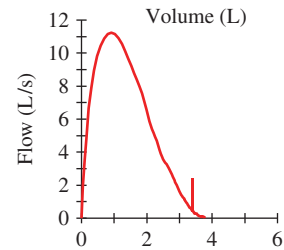
Commentary: This example is a little more complex. Both alveolar volume and carbon monoxide transfer factor are reduced – there is impairment to gas exchange. The transfer coefficient, KCO, provides little further information as it is within normal limits. The result may be due to loss of lung units (discrete or diffuse), poor gas mixing (gas trapping on SLV), parenchymal or pulmonary vascular disease or a combination of these. The overall results (including ventilatory function) point towards consideration of emphysema, though early interstitial lung disease due to amiodarone in addition to some airways obstruction should also be considered. Remember that a diagnosis should not be made using lung function test results alone and clinical correlation is required.

Case 9

Gender:	Male	Date:	26/10/2011
Age (yr):	65	Weight (kg):	81
Height (cm):	178	Race:	Caucasian

Clinical notes: Interstitial lung disease. ?progress

	Normal range	Baseline	*z*-score
Spirometry			
FEV_1 (L)	>2.66	3.41	−0.08
FVC (L)	>3.68	3.77	−1.49
FEV_1/FVC (%)	>65	90	+2.69
FEV_1/VC (%)	>65		
Single breath carbon monoxide transfer factor			
V_I (L)		3.68	
V_A (L)	>5.5	5.6	−1.49
T_LCO (mmol/min/kPa)	>6.5	5.0	−2.57
$T_LCO_{Hb\ corr}$ (mmol/min/kPa)		5.2	−2.46
KCO (mmol/min/kPa/L)	0.9–1.8	0.9	−1.90
$KCO_{Hb\ corr}$ (mmol/min/kPa/L)		0.9	−1.76
Hb (g/dL)		13.4	



Technical comment: Test performance was good.

Previous results:

Date	*26/10/11*[a]	*2/03/11*	*4/11/10*	*15/07/10*
FEV_1	3.41	3.61	4.10	4.20
FVC	3.77	4.10	4.84	4.95
FEV_1/FVC	90	88	85	85
V_A	5.6	5.5	6.4	6.5
T_LCO	5.0	5.9	6.8	7.7
$T_LCO_{Hb\ corr}$	5.2	5.9	6.9	8.2
KCO	0.9	1.1	1.1	1.2
$KCO_{Hb\ corr}$	0.9	1.1	1.1	1.3

[a] Current results.

(*continued*)

Cautionary statements:	The test is of good quality.
Technical interpretation:	Baseline spirometry is within normal limits. Alveolar volume is within normal limits and carbon monoxide transfer factor, corrected for haemoglobin, is reduced, suggestive of parenchymal or pulmonary vascular disease.
Clinical context:	In comparison to results from 2/3/2011, there has been no significant change in FEV_1, FVC or T_LCO. There has, however, been a progressive decline in FEV_1 (>200 mL and >12%), FVC (>200 mL and >12%) and T_LCO (>1.6 units, >10%) since tests from July 2010 (~15 months).

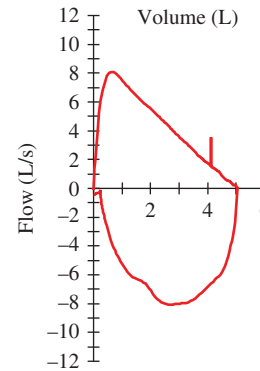
Final report: The test is of good quality. Baseline spirometry is within normal limits. Alveolar volume is within normal limits and carbon monoxide transfer factor, corrected for haemoglobin, is reduced, suggestive of parenchymal or pulmonary vascular disease. In comparison to results from 2/3/2011, there has been no significant change in FEV_1, FVC or T_LCO. There has, however, been a progressive decline in FEV_1, FVC and T_LCO compared to tests performed in July 2010 (~15 months). Results are consistent with known interstitial lung disease.
Commentary: This case has been chosen to illustrate reporting changes in T_LCO over time. This case highlights the importance of not only reviewing results with respect to the immediate prior result, but to look for changes over a longer period. The findings are typical of the pattern seen with interstitial lung disease.

Case 10

Gender:	Male	Date:	5/9/2010
Age (yr):	37	Weight (kg):	67.6
Height (cm):	172.4	Race:	Caucasian

Clinical notes: Post bone marrow transplant for Hodgkin's lymphoma. For review.

	Normal range	Baseline	*z*-score
Spirometry			
FEV_1 (L)	>3.29	4.15	+0.28
FVC (L)	>4.13	5.08	+0.14
FEV_1/FVC (%)	>71	82	+0.22
Single breath carbon monoxide transfer factor			
V_I (L)		4.84	
V_A (L)	>5.0	7.7	+1.55
T_LCO (mmol/min/kPa)	>8.3	10.6	−0.23
$T_LCO_{Hb\ corr}$ (mmol/min/kPa)		11.4	+0.23
KCO (mmol/min/kPa/L)	1.2–2.2	1.4	−1.34
$KCO_{Hb\ corr}$ (mmol/min/kPa/L)		1.5	−0.93
Hb (g/dL)		12.5	



Technical comment: Test performance was good.

Previous results:

Date	*5/09/10*[a]	*7/02/10*	*15/03/09*	*Pre bone marrow transplant 18/06/08*
FEV_1	4.15	3.99	4.13	4.35
FVC	5.08	5.09	4.9	5.03
FEV_1/FVC	82	78	84	86
V_A	7.7	7.1	7.0	7.3
T_LCO	10.6	8.7	8.6	7.2
$T_LCO_{Hb\ corr}$	11.4	9.5	9.8	8.3
KCO	1.4	1.2	1.2	1.0
$KCO_{Hb\ corr}$	1.5	1.3	1.4	1.1

[a] Current results.

(*continued*)

Cautionary statements:	The test is of good quality.
Technical interpretation:	Baseline spirometry is within normal limits. Carbon monoxide transfer factor, corrected for haemoglobin, is within normal limits.
Clinical context:	In comparison to results from 7/2/2010, there has been a significant increase in T_LCO (>1.6 units) with no significant change in FEV_1 or FVC.

Final report: The test is of good quality. Spirometry is within normal limits. Carbon monoxide transfer factor, corrected for haemoglobin, is within normal limits. In comparison to results from 7/2/2010, there has been a significant increase in T_LCO, with no significant change in FEV_1 or FVC.

Commentary: Graft versus host disease post bone marrow transplant can have a pulmonary presentation of a restrictive ventilatory defect and/or gas exchange impairment (reduced T_LCO). Many individuals have their lung function monitored post bone marrow transplant for this reason. In this example, the spirometry has remained stable and the T_LCO has improved over time. The clinical context in this case is the comparison of the current visit to previous results – the patient is presenting for review.

References

1 Macintyre N, Crapo RO, Viegi G, Johnson DC, van der Grinten CP, Brusasco V, et al. Standardisation of the single-breath determination of carbon monoxide uptake in the lung. Eur Respir J. 2005 Oct; 26(4):720–35.

2 Hughes JM, Pride NB. Examination of the Carbon Monoxide Diffusing Capacity (DLCO) in Relation to Its KCO and VA Components. Am J Respir Crit Care Med. 2012 Jul 15; 186(2):132–9.

3 Punjabi NM, Shade D, Wise RA. Correction of single-breath helium lung volumes in patients with airflow obstruction. Chest. 1998 Sep; 114(3):907–18.

4 Roberts CM, MacRae KD, Seed WA. Multi-breath and single breath helium dilution lung volumes as a test of airway obstruction. Eur Respir J. 1990 May; 3(5):515–20.

5 Pellegrino R, Viegi G, Brusasco V, Crapo RO, Burgos F, Casaburi R, et al. Interpretative strategies for lung function tests. Eur Respir J. 2005 Nov; 26(5):948–68.

6 van der Lee I, Zanen P, van den Bosch JM, Lammers JW. Pattern of diffusion disturbance related to clinical diagnosis: The K(CO) has no diagnostic value next to the DL(CO). Respir Med. 2006 Jan; 100(1):101–9.

7 Hughes JMB. Physiology and Practice of Pulmonary Function. Boldmere: The Association for Respiratory Technology and Physiology (ARTP); 2009.

8 Robson AG, Innes JA. Short term variability of single breath carbon monoxide transfer factor. Thorax. 2001 May; 56(5):358–61.

9 Hathaway EH, Tashkin DP, Simmons MS. Intraindividual variability in serial measurements of DLCO and alveolar volume over one year in eight healthy subjects using three independent measuring systems. Am Rev Respir Dis. 1989 Dec;140(6):1818–22.

CHAPTER 5

Tests of respiratory muscle strength

Respiratory muscle strength can be measured via a variety of techniques of varying technical difficulty and degrees of invasiveness (1). This chapter discusses the most commonly performed tests of respiratory muscle strength in standard clinical respiratory laboratories, the measurement of maximal respiratory pressures.

The maximal inspiratory pressure ($P_I$max or MIP) and maximal expiratory pressure ($P_E$max or MEP) are measurements of static pressure and reflect the maximum pressure generated by the respiratory muscles against an occluded airway and the elastic recoil pressure of the lung and chest wall (1, 2). In clinical practice, $P_I$max is usually measured following maximal exhalation, at or close to residual volume (RV), and $P_E$max following maximal inhalation, at or close to total lung capacity (TLC). Subjects perform a maximal inspiratory or expiratory effort against an occluded mouthpiece (with a small leak to reduce buccal muscle use and glottic closure) (1). Occasionally $P_I$max and $P_E$max may be measured from functional residual capacity (FRC) rather than TLC or RV. One study has shown that in healthy individuals, the differences in measured respiratory pressures at these different lung volumes are not clinically significant (3).

The sniff nasal inspiratory pressure (sNIP) is a more dynamic measure of inspiratory muscle strength. sNIP is a measure of the pressure generated via a maximal short, sharp inspiratory effort through an unobstructed nostril, generally from FRC. Pressure is measured via a catheter passed through a plug occluding the other nostril (1, 4).

Measures of maximal respiratory pressure assess global respiratory muscle function rather than specific muscles. The primary muscles used during

Interpreting Lung Function Tests: A Step-by-Step Guide, First Edition.
Brigitte M. Borg, Bruce R. Thompson and Robyn E. O'Hehir.
© 2014 John Wiley & Sons, Ltd. Published 2014 by John Wiley & Sons, Ltd.

active inspiration include the diaphragm, inspiratory intercostals, scalene and sternomastoid muscles. The abdominal wall muscles and expiratory intercostals are the primary muscles used during active expiration (2).

Test quality

Maximal respiratory pressures and sNIP are entirely effort-dependent tests. Poor volition, resulting in reduced values, may be due to submaximal effort or respiratory muscle dysfunction. Accurate technical comments regarding effort are crucial in this instance.

$P_I$max and $P_E$max (1):

- Acceptability criteria
  - — Maximal effort.
  - — $P_I$max – measured at or near the predetermined lung volume (RV or FRC).
  - — $P_E$max – measured at or near the predetermined lung volume (TLC or FRC).
  - — Must have tight lip seal.
  - — Support cheeks with hands during $P_E$max.
  - — Inspiratory and expiratory pressures must be maintained for at least 1.5 s, so that the mean pressure sustained over 1 s can be recorded.
  - — The peak pressure may be higher than mean pressure over the 1 s period; however, the peak pressure is believed to be less repeatable.
- Repeatability criteria
  - — Minimum of three acceptable efforts varying less than 20%.
- Maximal respiratory pressures will be affected by effort (reduced), leak around the mouthpiece (reduced) and orofacial muscle use (potentially increased).
- The type of mouthpiece used (flanged versus straight) will impact on results, with flanged mouthpiece producing slightly lower results compared to the straight mouthpiece. This should be taken into account when choosing reference values.

sNIP (1, 5):

- Acceptability criteria
  - — Measured at the end of relaxed expiration (FRC).
  - — Maximal effort.
  - — Smooth rise and sharp peak on pressure tracing.
- Repeatability criteria
  - — Minimum of 8–10 acceptable efforts, 3 highest within 10%.
- sNIP will be affected by effort, nasal obstruction and mouth leak.

Factors to consider during interpretation

- Respiratory muscles are used for many non-respiratory-related purposes (maintenance of posture, for example) and may have more strength than is required for respiration. Hence, despite there being deficits in maximal respiratory pressures, other aspects of lung function, such as vital capacity, may not be affected (1).
- Although a result in the normal range assists with excluding significant respiratory muscle dysfunction, an abnormal result may reflect poor test performance rather than reflecting true respiratory muscle weakness (1). Using multiple assessment methods for assessing respiratory muscle strength may be helpful in reducing the false positive rate for respiratory muscle weakness (6).
- $P_I$max may be reduced in isolation where obstruction with hyperinflation (of TLC) is present (see Chapter 4). In this case, the flattened diaphragm is at a mechanical disadvantage to generate maximal pressures (1).
- sNIP may be affected by obstructive lung disease because of the lack of equilibration of pressures across the lung (1, 2).

Interpretation

Parameters used in interpretation are as follows:
- $P_I$max – maximal inspiratory pressure (units: cmH_2O or kPa)
- $P_E$max – maximal expiratory pressure (units: cmH_2O or kPa)
- sNIP – sniff nasal inspiratory pressure (units: cmH_2O or kPa)

Additional parameters from other tests that may assist in assessing respiratory muscle strength include the following:
- VC: measured in both upright and supine postures
- Static lung volumes: TLC, RV and RV/TLC

Limits of the normal range are as follows:

- For $P_I$max, $P_E$max and sNIP, only abnormally low results are of interest. Therefore, the lower limit of normal (LLN) is set at a z-score of -1.64.
- Note: Reference values for maximal respiratory pressures ($P_I$max, $P_E$max) are varied and normal ranges are wide (1).
  - — Clinically significant inspiratory or expiratory muscle dysfunction can probably be excluded for absolute values of $P_I\text{max} > 80$ cmH_2O or $P_E\text{max} > 100$ cmH_2O, respectively (1, 2).
  - — Choose a reference set that used similar methodology to that used by the laboratory. The type of mouthpiece used makes a difference to values obtained (see Test Quality earlier).

Note: The normal ranges for sNIP are wide, possibly reflecting the wide range of normal muscle strength in individuals (1).

— Clinically significant inspiratory muscle weakness is unlikely to be present for absolute values of sNIP > 70 cmH_2O (males) and >60cm H_2O (females) (1). Keep in mind that sNIP represents the integrated pressure from all inspiratory muscles and there may be muscle weakness in individual muscles, which is unable to be detected using this test.

- See Chapters 2 and 3 for limits for spirometry and static lung volumes.

Table 5.1 outlines an interpretation strategy for maximal respiratory pressures using the LLN. An alternative interpretation strategy is that clinically significant inspiratory or expiratory muscle dysfunction can probably be excluded for absolute values of $P_I$max > 80 cmH_2O or $P_E$max > 100 cmH_2O, respectively (1, 2).

Other tests of respiratory function may also provide evidence of respiratory muscle dysfunction. However, the patterns seen are *not* specific for respiratory muscle dysfunction, and the results need to be interpreted in context with other findings and the clinical history of the subject. Examples include the following:

- A reduced VC is a common finding in significant respiratory muscle weakness.
- A reduced TLC and elevated RV/TLC (hence, reduced VC), particularly when there is no evidence of obstruction on spirometry (and often FRC is within the normal range), may indicate respiratory muscle dysfunction. The reduced TLC reflects the inability to fully inflate the lungs, and the elevated RV/TLC reflects the inability to fully exhale due to respiratory muscle weakness (1).
- A >30% fall in VC between upright and supine postures may suggest clinically significant diaphragm weakness (1).
- A reduced T_LCO and V_A may also occur in the presence of respiratory muscle weakness often with an elevated KCO (suggesting incomplete alveolar expansion), though this is not always the case (7).

Comparisons to previous results

The literature suggests that changes in $P_I$max and $P_E$max > 21–29 cmH_2O over weeks are considered clinically significant (in this book, changes >30 cmH_2O are considered significant) (8, 9). Changes >23 cmH_2O over a month are considered to be clinically significant for sNIP (8).

There is some evidence that change in $P_I$max between visits may, in part, be due to training effect rather than a physiological change, and this should also be taken into consideration. This difference is not observed using sNIP (10).

Table 5.1 Interpretative statements for measurement of respiratory muscle strength.

$P_I max$	$P_E max$	*sNIP*	*Interpretation*[a]
Within normal limits	Within normal limits		Maximal respiratory pressures are within normal limits, excluding clinically significant respiratory muscle dysfunction
<LLN	<LLN		Maximal respiratory pressures are reduced. This may reflect global respiratory muscle dysfunction[a]
<LLN	Within normal limits		The maximal inspiratory pressure is reduced in the presence of normal maximal expiratory pressure. This finding suggests inspiratory muscle weakness[b,c]
Within normal limits	<LLN		The maximal inspiratory pressure is within normal limits in the presence of a reduced maximal expiratory pressure. This finding suggests expiratory muscle weakness
		Within normal limits	Sniff nasal inspiratory pressure is within normal limits, excluding clinically significant inspiratory muscle weakness
		<LLN	Maximal inspiratory pressure is reduced. This may reflect inspiratory muscle weakness[c]

[a]Interpretative statements for measurement of respiratory muscle strength are provided in Table 5.1. The interpretation assumes that the test is of good quality and maximal effort has been achieved. When a value is less than the LLN, then consider the quality of the test. The low result may be due to poor effort rather than a true low result.
[b]$P_I$max may also be reduced in isolation in conditions where hyperinflation (of TLC) is present (see Chapter 3). In this case, the flattened diaphragm is at a mechanical disadvantage to generate maximal pressures, rather than the inspiratory muscles being weak.
[c]When both $P_I$max and sNIP are reduced, the likelihood of inspiratory muscle weakness increases.

Examples of interpretation of respiratory muscle strength

Respiratory muscle strength may be measured alone, but often is measured in conjunction with other tests. Interpretation is performed using the following steps as applicable:

1 Check for requirements of cautionary statements is related to the following parameters:

a. Reference values (are values appropriate for this subject? See Chapter 1 for details)

b. Quality of test (read technical comments, check raw data if required).

2 Read clinical notes.

3 Interpret parameters of lung function measured (e.g. spirometry, static lung volumes, gas transfer) with respect to standard patterns of abnormality and with respect to changes seen with respiratory muscle impairment.

4 Interpret measures of respiratory muscle strength.

5 Write technical interpretation (Table 5.1).

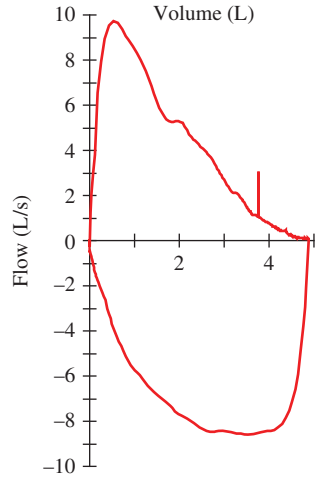
6 Compare current results to previous results.

7 Put results into clinical context.

Case 1

Gender:	Male				
Age (yr):	37	Weight (kg):	93		
Height (cm):	175	Race:	Caucasian		
Clinical notes:	Right diaphragm paralysis.				
	Normal range	Baseline	*z*-score	Supine	Change (%)
Spirometry					
FEV_1 (L)	>3.39	3.77	−0.83		
FVC (L)	>4.27	4.89	−0.51		
FEV_1/FVC (%)	>71	77	−0.57		
FEV_1/VC (%)	>71	75			
VC (L)	>4.27	5.04	+0.24	4.63	−8.0
Maximal respiratory pressures					
$P_I$max (cmH_2O)	>76	133	+0.05		
$P_E$max (cmH_2O)	>104	162	+0.42		

Technical comment: Test performance was good.



Cautionary statements: The test is of good quality.

Technical interpretation: Baseline ventilatory function is within normal limits. Maximal respiratory pressures are within normal limits, excluding respiratory muscle weakness. The difference between upright and supine VC is <30%, suggesting no significant diaphragm dysfunction.

Clinical context: Results suggest that known right diaphragm paralysis is not significantly impacting on ventilatory function.

Final report: The test is of good quality. Baseline ventilatory function is within normal limits. Maximal respiratory pressures and the assessment of diaphragm function using upright and supine VCs are within normal limits. Results suggest that the known right diaphragm paralysis is not significantly impacting on respiratory function at this time.

Commentary: In this case, diaphragm function has been assessed using maximal respiratory pressures – an assessment of global respiratory muscle function, and using upright and supine measures of VC – a more specific assessment of diaphragm function. Falls in VC from upright to supine postures are expected in healthy subjects (up to 15%). Large falls are required (>30%) to be considered clinically significant (1). All assessments in this case are within normal limits.

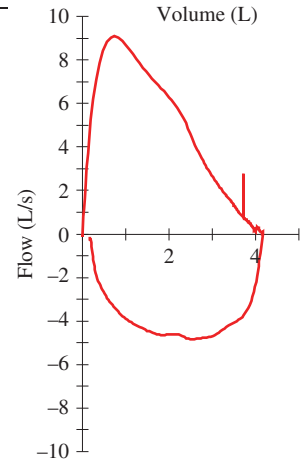
Case 2

Gender:	Male		
Age (yr):	25	Weight (kg):	76
Height (cm):	186	Race:	Caucasian

Clinical notes: Myotonic dystrophy.

	Normal range	Baseline	*z*-score
Spirometry			
FEV_1 (L)	>4.14	3.73	−2.42
FVC (L)	>5.08	4.17	−3.12
FEV_1/FVC (%)	>73	89	+1.11
Static lung volumes			
TLC (L)	5.98–9.09	5.95	−2.00
RV (L)	<2.31	1.90	+0.55
FRC (L)	2.31–5.12	3.58	−0.19
RV/TLC (%)	<29	32	+2.33
VC (L)	>5.08	4.05	
Maximal respiratory pressures			
$P_I$max (cmH_2O)	>74	46	−3.07
$P_E$max (cmH_2O)	>101	48	−5.14

Technical comment: Test performance was good.



Cautionary statements: The test is of good quality.

Technical interpretation: There is a restrictive ventilatory defect on spirometry, confirmed by a reduced TLC (just). Maximal respiratory pressures are reduced and suggest global respiratory muscle weakness. Note that RV/TLC is elevated, further suggesting respiratory muscle weakness rather than airflow limitation as there is no evidence of obstruction on spirometry.

Clinical context: Results suggest a restrictive ventilatory defect and respiratory muscle weakness, consistent with known myotonic dystrophy.

Final report: The test is of good quality. There is a restrictive ventilatory defect. Maximal respiratory pressures are reduced suggesting global respiratory muscle weakness. The elevated RV/TLC suggests respiratory muscle weakness rather than obstruction as there is no evidence of obstruction on spirometry. Results are consistent with known myotonic dystrophy.

Commentary: In this case, the elevated RV/TLC is more likely to be due to respiratory muscle weakness (subject unable to maximally fill and empty their lungs) than gas trapping due to airflow limitation as there is no evidence of obstruction on spirometry. Note: FRC is within normal limits also.

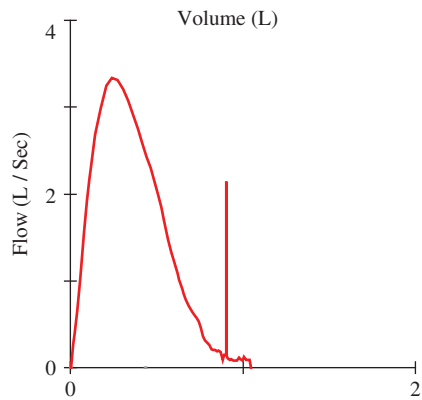
Case 3

Gender:	Female		
Age (yr):	51	Weight (kg):	58
Height (cm):	153	Race:	Caucasian

Clinical notes: Amyloid myopathy

	Normal range	Baseline	*z*-score	Supine	Change (%)
Spirometry					
FEV_1 (L)	>1.92	0.91	−4.84		
FVC (L)	>2.46	1.05	−5.43		
FEV_1/FVC (%)	>70	87	+1.12		
VC (L)	>2.46	1.05	−5.43	0.72	−31
Maximal respiratory pressures					
$P_I$max (cmH_2O)	>42	33	−2.39		
$P_E$max (cmH_2O)	>65	82	−0.53		
sNIP (cmH_2O)	>56	45	−2.26		

Technical comment: Test performance was good.



Cautionary statements: The test is of good quality.

Technical interpretation: There appears to be a restrictive ventilatory defect. Static lung volumes are required to confirm restriction. MIP and sNIPs are reduced, while maximal expiratory pressure is within normal limits, suggesting inspiratory respiratory muscle weakness. The fall in vital capacity between upright and supine posture (>30%) suggests clinically significant diaphragm weakness.

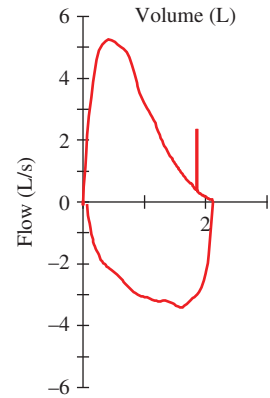
Clinical context: Results suggest inspiratory respiratory muscle weakness with impaired ventilatory function.

Final report: The test is of good quality. There appears to be a restrictive ventilatory defect. Measurement of static lung volumes is suggested to confirm restriction. Maximal and sniff nasal inspiratory pressures are reduced, while maximal expiratory pressure is within normal limits, suggesting inspiratory respiratory muscle weakness. The fall in vital capacity between upright and supine postures suggests clinically significant diaphragm weakness. There is impairment of ventilatory function with evidence of inspiratory respiratory muscle weakness.
Commentary: In this case, three assessments of inspiratory respiratory muscle function have been performed ($P_I$max, sNIP and upright and supine measures of vital capacity). The likelihood of inspiratory muscle dysfunction is increased as the findings are abnormal for all three measures.

Case 4

Gender:	Female		
Age (yr):	34	Weight (kg):	56.6
Height (cm):	153	Race:	Caucasian
Clinical notes:	Polymyositis affecting heart and muscles. ?respiratory muscle involvement.		

	Normal range	Baseline	*z*-score
Spirometry			
FEV_1 (L)	>2.26	1.87	−2.88
FVC (L)	>2.69	2.11	−3.21
FEV_1/FVC (%)	>74	89	+0.85
Static lung volumes			
TLC (L)	3.44–5.54	3.00	−2.78
RV (L)	<1.90	0.98	−0.78
FRC (L)	1.41–3.46	1.51	−1.76
RV/TLC (%)	<37	33	+0.83
VC (L)	>2.69	2.02	
Single breath carbon monoxide transfer factor			
V_I (L)		2.04	
V_A (L)	>3.3	2.9	−2.31
T_LCO (mmol/min/kPa)	>5.5	5.2	−1.87
$T_L CO_{Hb\ corr}$ (mmol/min/kPa)		5.3	−1.83
KCO (mmol/min/kPa/L)	1.2–2.2	1.8	+0.44
$KCO_{Hb\ corr}$ (mmol/min/kPa/L)		1.8	+0.51
Hb (g/dL)		13.1	



	Normal range	Baseline	*z*-score
Maximal respiratory pressures			
$P_I$max (cmH_2O)	>45	48	−1.45
$P_E$max (cmH_2O)	>68	53	−2.83
sNIP (cmH_2O)	>59	75	−0.73
Technical comment:		Test performance was good.	

Cautionary statements: The test is of good quality.

Technical interpretation: There appears to be a restrictive ventilatory defect on spirometry. Restriction is confirmed on static lung volumes. Both V_A and T_LCO, corrected for haemoglobin, are reduced. KCO is within the normal range, therefore the reduction in T_LCO may be due to the reduced V_A, parenchymal or pulmonary vascular disease or a combination of these. MIP and sNIPs are within normal limits, while maximal expiratory pressure is reduced, suggesting expiratory respiratory muscle weakness. Technical comment reports good quality test, therefore submaximal effort is unlikely to be responsible for reduced $P_E$max.

Clinical context: Results suggest a restrictive ventilatory defect with gas exchange impairment and expiratory respiratory muscle weakness.

Final report: The test is of good quality. There is a restrictive ventilatory defect. Both alveolar volume and carbon monoxide transfer factor, corrected for haemoglobin, are reduced. The reduction in T_LCO may be due to the reduced V_A, parenchymal or pulmonary vascular disease or a combination of these. Maximal and sniff nasal inspiratory pressures are within normal limits, while maximal expiratory pressure is reduced, suggesting expiratory respiratory muscle weakness. Results suggest a restrictive ventilatory defect with gas exchange impairment of uncertain cause and expiratory respiratory muscle weakness.

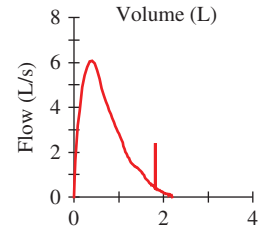
Commentary: This case suggests expiratory muscle weakness with what appears to be intact inspiratory muscle function (both $P_I$max and sNIP within normal limits). There is a restrictive ventilatory defect with gas exchange impairment also. As KCO is within normal limits, the reduction in T_LCO may not be due to respiratory muscle weakness alone. Pulmonary presentations for myositis include interstitial lung disease and respiratory muscle weakness (11). In this case, interstitial lung disease should also be considered.

Case 5

Gender:	Male	Date:	4/7/2011
Age (yr):	58	Weight (kg):	92.9
Height (cm):	172	Race:	Caucasian

Clinical notes: Severe systemic lupus erythematosus (SLE). Myopathy for review.

	Normal range	Baseline	*z*-score
Spirometry			
FEV_1 (L)	>2.65	1.83	−3.48
FVC (L)	>3.58	2.19	−4.27
FEV_1/FVC (%)	>66	84	+1.27
FEV_1/VC (%)	>66	72	−0.73
Static lung volumes			
TLC (L)	4.97–8.08	4.03	−3.15
RV (L)	<2.69	1.48	−1.59
FRC (L)	1.94–4.76	1.96	−1.94
RV/TLC (%)	<39	37	+1.15
VC (L)	>3.58	2.55	−3.59
Single breath carbon monoxide transfer factor			
V_I (L)		2.21	
V_A (L)	>5.2	3.6	−3.93
T_LCO (mmol/min/kPa)	>6.9	6.4	−2.11
$T_LCO_{Hb\ corr}$ (mmol/min/kPa)		6.7	−1.87
KCO (mmol/min/kPa/L)	1.1–1.8	1.8	+2.05
$KCO_{Hb\ corr}$ (mmol/min/kPa/L)		1.9	+2.55
Hb (g/dL)		13.1	
Maximal respiratory pressures			
$P_I$max (cmH_2O)	>69	48	−2.72
$P_E$max (cmH_2O)	>103	98	−1.87



Technical comment: Test performance was good.

Previous results:

Date	*4/7/2011*[a]	*5/1/2011*	*7/10/2010*	*27/6/2010*
FEV_1	1.83	1.76	1.58	1.47
FVC	2.19	2.27	2.07	1.73
FEV_1/FVC	72	78	76	86
TLC	4.03	3.83	3.54	3.37
RV	1.48	1.34	1.51	1.36
FRC	1.96	1.97	2.21	2.29
$P_I$max	48	53	42	45
$P_E$max	98	106	99	96

[a]Current visit.

Cautionary statements: The test is of good quality.

Technical interpretation: There appears to be a restrictive ventilatory defect on spirometry confirmed by static lung volumes. Both V_A and T_LCO, corrected for haemoglobin, are reduced. Results suggest that the reduction in T_LCO is likely to be due to the reduced V_A (KCO elevated). Maximal respiratory pressures are reduced, suggesting respiratory muscle weakness.

Clinical context: In comparison to results from the 5/1/2011, there has been no significant change. There has, however, been a significant increase in FEV_1 and FVC in comparison to results from ~1 year ago (27/6/2010).

Final report: The test is of good quality. There is a restrictive ventilatory defect. Both alveolar volume and carbon monoxide transfer factor, corrected for haemoglobin, are reduced. Results suggest that reduced T_LCO is likely to be due to the reduction in V_A. Maximal respiratory pressures are reduced, suggesting respiratory muscle weakness. In comparison to previous results from 5/1/2011, there has been no significant change in respiratory muscle strength, FEV_1 or FVC. There has, however, been a significant increase in FEV_1 and FVC in comparison to results from a year ago (27/6/2010). Results suggest a restrictive ventilatory defect with gas exchange impairment, possibly due to respiratory muscle weakness, though clinical correlation is required.

Commentary: SLE has a number of respiratory presentations (12), of which respiratory muscle dysfunction is one. The presentation in this case appears to be consistent with the pulmonary presentation referred to as 'shrinking lung syndrome' (12). The presentation of shrinking lung syndrome is restriction due to respiratory muscle impairment. T_LCO is generally not implicated, but may become impaired due to failure to breathe in sufficiently (as this case demonstrates – reduced T_LCO with elevated KCO). That is, it is the impairment of the respiratory pump muscles

that results in impaired gas exchange rather than parenchymal or pulmonary vascular abnormalities causing the gas exchange impairment. Note that parenchymal or pulmonary vascular abnormalities can be found in other respiratory presentations of SLE (12).

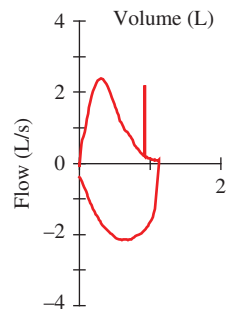
Case 6

Gender:	Female	Date:	25/10/2010
Age (yr):	53	Weight (kg):	69.8
Height (cm):	157.8	Race:	Caucasian

Clinical notes: Cough and dyspnoea. Phrenic nerve damaged 18 months ago during surgery to repair mitral valve. For review.

	Normal range	Baseline	*z*-score	Supine	Change (%)
Spirometry					
FEV_1 (L)	>2.01	0.94	−4.83		
FVC (L)	>2.60	1.13	−5.35		
FEV_1/FVC (%)	>70	83	+0.61		
VC (L)	>2.60	1.13	−5.35	0.69	−39
Static lung volumes					
TLC (L)	3.72–5.82	2.72	−3.83		
RV (L)	<2.38	1.64	−0.30		
FRC (L)	1.64–3.69	1.76	−1.73		
RV/TLC (%)	<45	60	+4.32		
Maximal respiratory pressures					
$P_I$max (cmH_2O)	>46	42	−1.90		
$P_E$max (cmH_2O)	>67	58	−2.33		

Technical comment: Test performance was good.



Previous results:

Date	*25/10/2010*[a]	*20/2/2010*	*30/8/2009*
FEV_1	0.94	0.92	0.92
FVC	1.13	1.13	1.16
FEV_1/FVC	83	81	79
TLC	2.72	3.11	2.83
RV	1.64	1.78	1.59
FRC	1.76	1.98	1.97
$P_I$max	42	32	47
$P_E$max	58	39	69

[a]Current visit.

Cautionary statements: The test is of good quality.

Technical interpretation: There appears to be a restrictive ventilatory defect on spirometry confirmed by static lung volumes. RV/TLC is elevated and, in the setting of no evidence of obstruction on spirometry, suggests respiratory muscle dysfunction. This is supported by the reduction in maximal respiratory pressures signifying global respiratory muscle weakness. The fall in VC between upright and supine postures suggests clinically significant diaphragm weakness.

Clinical context: In comparison to results from the 20/2/2010 and 30/8/2009, there has been no significant change.

Final report: The test is of good quality. There is a restrictive ventilatory defect. Maximal respiratory pressures are reduced, suggesting global respiratory muscle weakness. The fall in vital capacity between upright and supine postures suggests clinically significant diaphragm weakness. In comparison to results from 20/2/2010 and 30/8/2009, there has been no significant change in spirometry or maximal respiratory pressures.

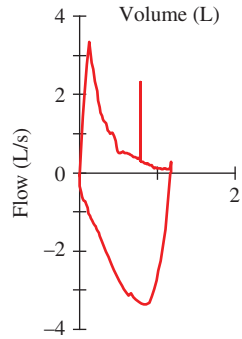
Commentary: Similarly to Case 2, the elevated RV/TLC in this case is more likely to be related to respiratory muscle dysfunction than airway obstruction as there is no evidence of obstruction on spirometry. The TLC is reduced out of proportion to the reduction in RV, suggesting the subject is unable to completely inhale or exhale due to respiratory muscle limitation.

Case 7

Gender:	Female		
Age (yr):	52	Weight (kg):	80
Height (cm):	157	Race:	Caucasian
Clinical notes:	COPD, OSA.		

	Normal range	Baseline	*z*-score	Post-BD	Change (%)
Spirometry					
FEV_1 (L)	>2.01	0.79	−5.32	0.85	+8
FVC (L)	>2.59	1.21	−5.16	1.24	+2
FEV_1/FVC (%)	>70	65	−2.43	69	
FEV_1/VC (%)	>70	64	−2.70		
Static lung volumes					
TLC (L)	3.68–5.78	3.27	−2.72		
RV (L)	<2.34	2.03	+0.82		
FRC (L)	1.61–3.66	2.42	−0.40		
RV/TLC (%)	<45	62	+4.77		
VC (L)	>2.59	1.24			
Single breath carbon monoxide transfer factor					
V_I (L)		0.94			
V_A (L)	>3.7	1.8	−5.05		
T_LCO (mmol/min/kPa)	>5.4	2.6	−4.68		
$T_LCO_{Hb\ corr}$ (mmol/min/kPa)		2.8	−4.46		
KCO (mmol/min/kPa/L)	1.1–1.9	1.4	−0.19		
$KCO_{Hb\ corr}$ (mmol/min/kPa/L)		1.5	+0.31		
Hb (g/dL)		11.4			
Maximal respiratory pressures					
$P_I$max (cmH_2O)	>49	35	−2.63		
$P_E$max (cmH_2O)	>69	119	+0.89		
sNIP (cmH_2O)	>55	67	−0.96		

Technical comment: Test performance was good.



Cautionary statements: The test is of good quality.

Technical interpretation: There is an obstructive ventilatory defect with a reduced FVC. The response to inhaled bronchodilator is not significant. Static lung volumes suggest a concomitant restrictive defect with evidence of gas trapping. Both alveolar volume and T_LCO, corrected for haemoglobin, are reduced. Results suggest that the reduction in T_LCO may be due to the reduction in V_A, parenchymal or pulmonary vascular disease or a combination of these (KCO is within normal limits). The maximal expiratory pressure is within normal limits. The MIP is reduced. However, sNIP is within normal limits, making clinically significant inspiratory respiratory muscle weakness unlikely.

Clinical context: Results suggest a mixed obstructive/restrictive ventilatory pattern with gas exchange impairment. Respiratory muscle function appears to be intact.

Final report: The test is of good quality. There is a mixed obstructive/restrictive ventilatory defect with no significant response to inhaled bronchodilator. Both alveolar volume and carbon monoxide transfer factor, corrected for haemoglobin, are reduced. Results suggest that the reduction in T_LCO may be due to the reduction in V_A, parenchymal or pulmonary vascular disease or a combination of these. The maximal expiratory pressure is within normal limits and the MIP is reduced. sNIP is, however, in the normal range, making clinically significant inspiratory respiratory muscle weakness unlikely. Results suggest a mixed obstructive/restrictive ventilatory defect with gas exchange impairment. Respiratory muscle function appears to be intact.

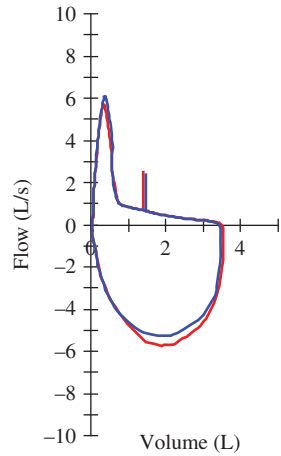
Commentary: In this case, $P_I$max and sNIP, two measures of inspiratory muscle strength, have contrary results with abnormal and normal findings, respectively. A normal finding in one measure generally outweighs an abnormal finding in tests assessing respiratory muscle function (6).

Case 8

Gender:	Male		
Age (yr):	63	Weight (kg):	85
Height (cm):	171	Race:	Caucasian
Clinical notes:	COPD, increasing breathlessness.		

	Normal range	Baseline	*z*-score	Post-BD	Change (%)
Spirometry					
FEV_1 (L)	>2.44	1.40	−4.00	1.42	+1
FVC (L)	>3.37	3.58	−1.24	3.49	−3
FEV_1/FVC (%)	>65	39	−6.11	41	
FEV_1/VC (%)	>65	36	−6.62		
Static lung volumes					
TLC (L)	4.91–8.02	8.52	+2.60		
RV (L)	<2.77	4.64	+6.64		
FRC (L)	1.94–4.76	7.13	+5.27		
RV/TLC (%)	<41	49	+3.53		
VC (L)	>3.37	3.88			
Single breath carbon monoxide transfer factor					
V_I (L)		3.23			
V_A (L)	>5.1	5.2	−1.53		
T_LCO (mmol/min/kPa)	>6.6	4.4	−3.43		
$T_LCO_{Hb\ corr}$ (mmol/min/kPa)		4.9	−3.00		
KCO (mmol/min/kPa/L)	1.0–1.7	0.8	−3.12		
$KCO_{Hb\ corr}$ (mmol/min/kPa/L)		0.9	−2.50		
Hb (g/dL)		11.2			
Maximal respiratory pressures					
$P_I$max (cmH_2O)	>64	59	−1.91		
$P_E$max (cmH_2O)	>100	121	−0.76		

Technical comment: Test performance was good.



Cautionary statements: The test is of good quality.

Technical interpretation: There is an obstructive ventilatory defect. The response to inhaled bronchodilator is not significant. Static lung volumes suggest hyperinflation (TLC). Alveolar volume is within normal limits and T_LCO, corrected for haemoglobin is reduced, suggestive of parenchymal or pulmonary vascular disease. The maximal expiratory pressure is within normal limits, while MIP is reduced, suggesting inspiratory muscle dysfunction.

Clinical context: Spirometry results are consistent with the definition of COPD, and there is evidence of gas exchange impairment. There is some evidence of inspiratory respiratory muscle dysfunction, which may be due to weakness or mechanical disadvantage due to hyperinflation (TLC).

Final report: The test is of good quality. There is an obstructive ventilatory defect with no significant response to inhaled bronchodilator. Static lung volumes suggest hyperinflation (TLC). Alveolar volume within normal limits and T_LCO, corrected for haemoglobin, is reduced, suggestive of parenchymal or pulmonary vascular disease. Maximal expiratory pressure is within normal limits, while MIP is reduced, suggesting inspiratory muscle dysfunction. Spirometry results are consistent with the definition of COPD, and there is evidence of gas exchange impairment. There is some evidence of inspiratory respiratory muscle dysfunction, which may be due to weakness or mechanical disadvantage due to hyperinflation (TLC). Clinical correlation is required.

Commentary: In this case, the reduction in inspiratory pressures may be due to the hyperinflation related to COPD. Hyperinflation may lead to flattening of the diaphragm, placing it at a mechanical disadvantage.

References

1 ATS/ERS Statement on respiratory muscle testing. Am J Respir Crit Care Med. 2002 Aug 15; 166(4):518–624; http://www.thoracic.org/statements/resources/pft/respmuscle.pdf [accessed 21 March 2014].

2 Gibson GJ. Measurement of respiratory muscle strength. Respir Med. 1995 Sep; 89(8):529–35.

3 Bruschi C, Cerveri I, Zoia MC, Fanfulla F, Fiorentini M, Casali L, et al. Reference values of maximal respiratory mouth pressures: a population-based study. Am Rev Respir Dis. 1992 Sep; 146(3):790–3.

4 Troosters T, Gosselink R, Decramer M. Chapter 4. Respiratory muscle assessment European Respiratory Society Monograph 2005; 31 (Lung Function Testing): 57–71.

5 Heritier F, Rahm F, Pasche P, Fitting JW. Sniff nasal inspiratory pressure. A noninvasive assessment of inspiratory muscle strength. Am J Respir Crit Care Med. 1994 Dec; 150(6 Pt 1):1678–83.

6 Steier J, Kaul S, Seymour J, Jolley C, Rafferty G, Man W, et al. The value of multiple tests of respiratory muscle strength. Thorax. 2007 Nov; 62(11):975–80.

7 Hart N, Cramer D, Ward SP, Nickol AH, Moxham J, Polkey MI, et al. Effect of pattern and severity of respiratory muscle weakness on carbon monoxide gas transfer and lung volumes. Eur Respir J. 2002 Oct; 20(4):996–1002.

8 Maillard JO, Burdet L, van Melle G, Fitting JW. Reproducibility of twitch mouth pressure, sniff nasal inspiratory pressure, and maximal inspiratory pressure. Eur Respir J. 1998 Apr; 11(4):901–5.

9 Dimitriadis Z, Kapreli E, Konstantinidou I, Oldham J, Strimpakos N. Test/retest reliability of maximum mouth pressure measurements with the MicroRPM in healthy volunteers. Respir Care. 2011 Jun; 56(6):776–82.

10 Terzi N, Corne F, Mouadil A, Lofaso F, Normand H. Mouth and nasal inspiratory pressure: learning effect and reproducibility in healthy adults. Respiration. 2010; 80(5):379–86.

11 Kalluri M, Oddis CV. Pulmonary manifestations of the idiopathic inflammatory myopathies. Clin Chest Med. 2010 Sep; 31(3):501–12.

12 Carmier D, Marchand-Adam S, Diot P, Diot E. Respiratory involvement in systemic lupus erythematosus. Rev Mal Respir. 2010 Oct; 27(8):e66–78.

CHAPTER 6

Bronchial provocation tests

Bronchial provocation tests assist in identifying airway hyper-responsiveness (AHR – a major feature of asthma) in individuals who have normal spirometry with no bronchodilator (BD) reversibility but have symptoms consistent with asthma.

There are multiple protocols for bronchial provocation tests using multiple stimuli, modes of administration and threshold doses for determining AHR. This chapter reviews the principles of reporting bronchial provocation tests using a number of different methods and stimuli; however, it is necessary to keep in mind that the methods and concentrations/doses of provoking stimuli used in this chapter may not reflect those of your local environment.

Bronchial provocation tests can be divided into two types: direct and indirect challenges.

- Direct challenges
  - — Act on airway smooth muscle receptors to cause bronchoconstriction (1, 2).
  - — Inhalation agents include methacholine and histamine.
  - — Note: AHR associated with direct challenges may also reflect lung injury not associated with asthma.
- Indirect challenges
  - — Act by causing the release of inflammatory mediators which act on airway smooth muscle receptors to cause bronchoconstriction (1, 3).
  - — Provide information regarding current airway inflammation.
  - — Inhalation agents include mannitol, hypertonic saline and adenosine monophosphate.
  - — Physical challenges include eucapnic voluntary hyperpnea or hyperventilation (EVH), exercise.

Interpreting Lung Function Tests: A Step-by-Step Guide, First Edition.
Brigitte M. Borg, Bruce R. Thompson and Robyn E. O'Hehir.
© 2014 John Wiley & Sons, Ltd. Published 2014 by John Wiley & Sons, Ltd.

Test procedure:

Inhalation challenges are generally stepped cumulative dose challenges (4, 5) with an upper limit of stimuli delivered. That is, following baseline spirometry, the provoking stimulus is delivered to the airways in steps, with FEV_1 measured after each stage. The test is performed within a prescribed time frame to ensure the cumulative effect of the stimulus. A dose–response curve can be constructed by plotting FEV_1 against the cumulative dose.

Physical challenges are generally single-dose challenges (5, 6). That is, spirometry (FEV_1) is measured before (baseline) and at regular intervals up to 15–30 min after a single provoking stimulus (for example, 6 min of voluntary hyperventilation of a dry gas mixture). A dose–response curve cannot be constructed for single-stimulus dose tests.

Airway responsiveness to the provoking stimulus is described as the stimulus dose or concentration required to provoke a predetermined percentage fall in FEV_1. The percentage fall in FEV_1 varies dependent on the provoking stimulus (see Table 6.2).

Where a provoking dose (PD) can be calculated (stepped challenge tests), the PD is notated as PDxx, where xx is the per cent fall in FEV_1 that identifies a positive challenge (or AHR). For example: for methacholine challenges, the PD is notated as PD_{20}, as a 20% fall in FEV_1 is required for the airways to be considered hyper-responsive.

Table 6.1 Medications, foods and other to be avoided prior to challenges.

Direct challenges: (4)	*Time withheld*
Short-acting inhaled bronchodilators	8 h
Medium-acting bronchodilators	24 h
Long-acting inhaled bronchodilators	48 h
Intermediate-acting theophyllines	24 h
Long-acting theophyllines	48 h
Standard beta-2 agonist tablets	12 h
Cromolyn sodium	8 h
Mast cell stabilizers	48 h
Antihistamines	3 days
Leukotriene antagonists	24 h
Caffeine containing food and drink	Day of test
Indirect challenges, as for direct challenges plus: (1, 5)	
Leukotriene antagonists	4 days
Vigorous exercise	4 h, preferably day of test
Corticosteroids (when looking for effectiveness of therapy)	Day of test
Corticosteroids (when looking for diagnosis)	Up to 6 weeks

A note about methacholine challenges

There are multiple methods and dosing limits for methacholine challenges (4, 7, 8). Some methods involve tidal breathing, while others use dosimeters to deliver a known dose to the airway via multiple single inspiratory breaths. Evidence suggests that the methods are probably not interchangeable and an individual may be responsive to one method, but not another (9). The method of administering methacholine determines whether a provoking dose or a provoking concentration is calculated.

Test quality

Bronchodilators, corticosteroids (inhaled or oral), antihistamines and some foods (e.g. coffee) may affect AHR and these should be avoided prior to bronchial provocation tests (see Table 6.1).

The inability to meet acceptability and repeatability criteria for spirometry will affect test quality and result interpretation (see Chapter 2). An inability to inhale the provoking stimulus (or ventilate sufficiently in the case of physical challenges) also may deliver inconclusive findings.

Interpretation

Steps:

1 Check medications, foods and exercise have been withheld/avoided as appropriate. Comment as necessary.

2 Check quality of spirometry results. Comment as necessary.

3 Assess baseline spirometry (see Chapter 2): baseline airflow obstruction can result in false-positive results with direct challenges and findings must be interpreted cautiously in this situation (4).

4 Evaluate challenge results (see Table 6.2).

Determine the likelihood of bronchoconstriction or asthma using sensitivity/specificity data (see Table 6.3).

— Keep in mind that the diagnosis of asthma is usually made by the referring physician in the light of a variety of findings including symptoms, clinical assessment and physiological assessment. A challenge test is only one element in the decision-making strategy.

— There is no 'gold standard' against which to measure sensitivity and specificity of different challenges (9). Most often it is measured against a clinical diagnosis of asthma (doctor diagnosed). Differences in methods of administration using the same provoking agent may result in differences in specificity/sensitivity (9).

— Individuals may be positive to one type of challenge but not another (10).

5 Add clinical context, if possible, taking into consideration medication use.

— Table 6.4 describes the clinical context for mannitol and hypertonic saline results with use of inhaled corticosteroids (ICSs).

— ICSs may reduce AHR or in some cases eliminate AHR in response to methacholine challenge, but results are inconsistent (4). Direct challenges are not considered to be useful for assessing response to ICS therapy (9).

Severity scales

Severity scales for methacholine, hypertonic saline, mannitol and eucapnic voluntary hyperventilation challenges are available (4, 5), though are not used in this book.

Table 6.2 Factors for determining if a bronchial provocation test result is positive, negative or inconclusive.

Provoking stimulus (provoking dose/ concentration)	*Response*	*Requirement*
Methacholine (4) (PD_{20} or PC_{20})	Positive	≥20% drop from baseline FEV_1 after inhalation of diluent or ≥20% drop in FEV_1[a] and $PD_{20} < 2$ mg[b] or $PC_{20} < 16$ mg/mL[b]
	Negative	<20% drop in FEV_1[a] and $PD_{20} > 2$ mg[b] or $PC_{20} > 16$ mg/mL[b]
Hypertonic saline (5) (PD_{15})	Positive	≥15% drop from baseline FEV_1 and $PD_{15} < 23.5$ mL
	Negative	<15% drop from baseline FEV_1 and $PD_{15} > 23.5$ mL or ≥15% drop from baseline FEV_1 and $PD_{15} > 23.5$ mL
	Inconclusive	<15% drop from baseline FEV_1 and <23.5 mL saline delivered

Table 6.2 (*continued*)

Provoking stimulus (provoking dose/ concentration)	*Response*	*Requirement*
Mannitol (5, 11) (PD_{15})	Positive	≥15% drop from baseline FEV_1 and PD_{15} < 635 mg or ≥10% drop in FEV_1 between consecutive doses
	Negative	<15% drop from baseline FEV_1 and PD_{15} ≥ 635 mg
	Inconclusive	<15% drop from baseline FEV_1 and <635 mg mannitol inhaled
EVH (5) (no provoking dose for EVH)	Positive	≥10% drop from baseline FEV_1
	Negative	<10% drop from baseline FEV_1 and target ventilation was maintained (>85% MVV)
	Inconclusive	<10% drop from baseline FEV_1 and target ventilation not maintained (<85% MVV)
Exercise (5) (no provoking dose for exercise)	Positive	Paediatrics > 13% fall from baseline FEV_1 Adults > 10% fall from baseline FEV_1 Elite athletes > 7% fall from baseline FEV_1
	Negative or inconclusive	A challenge that is not positive may be inconclusive rather than negative due to difficulties in ensuring that subjects exercise at sufficient intensity to achieve and sustain adequate ventilation to provoke exercise-induced bronchoconstriction

PD, provoking dose; MVV, maximum voluntary ventilation.
[a] Using post-diluent FEV_1 as reference point.
[b] Maximum dose/concentration delivered varies according to method used. Check what your local laboratory uses as the maximal dose/concentration.

Comparisons to previous results

There is little in the literature regarding the value of interchallenge variation over time as part of the interpretation strategy.

The repeatability of the majority of stepped dose bronchial provocation tests is within one to two doubling doses (1, 14), suggesting that changes of more than two doubling doses may be clinically important. Similarly, a repeated challenge that moves from positive to negative (or vice versa) is probably a clinically important change.

Table 6.3 Sensitivity/specificity of challenge tests for a diagnosis of asthma.

Provoking agent	*Sensitivity/specificity (compared to a clinical diagnosis of asthma)*	*Comments*
Direct challenges		
Methacholine (4, 10)	High sensitivity	A negative challenge excludes AHR, but not exercise-induced bronchoconstriction
	Low specificity	A positive challenge indicates AHR, but is not specific for asthma
Indirect challenges		
Mannitol and Hypertonic saline (10, 11)	Low sensitivity	Unable to rule out asthma with a negative challenge
	High specificity	Positive result is highly specific for asthma
Physical challenges		
EVH, Exercise (10, 12, 13)	Low sensitivity	Unable to rule out asthma with a negative challenge
	High specificity	Positive result is highly specific for exercise-induced asthma

Table 6.4 Clinical context for indirect challenges.

For mannitol and hypertonic saline bronchial provocation tests (3, 11):		
Result	*Using ICS?*	*Clinical context*
Positive	No	Consistent with asthma with active airway inflammation
Positive	Yes	Consistent with asthma with suboptimal control of airway inflammation
Negative	No	Asthma cannot be excluded. Consider further investigation if clinically indicated or an alternate diagnosis
Negative	Yes	Consistent with asthma with controlled airway inflammation or consider an alternate diagnosis

ICS, inhaled corticosteroid.

Examples of interpretation of bronchial provocation challenges

Case 1

Gender:	Female		
Age (yr):	46	Weight (kg):	73.4
Height (cm):	173	Race:	Caucasian

Clinical notes: Paroxysmal shortness of breath. For investigation.

	Normal range	Baseline	*z*-score
Spirometry			
FEV_1 (L)	>2.64	3.52	0.55
FVC (L)	>3.35	4.67	1.13
FEV_1/FVC (%)	>71	75	−0.95

Challenge: Methacholine (dosimeter)

Dose (mg)	saline	0.016	0.063	0.250	1.0	2.0	Post-BD
FEV_1 (L)	3.28	3.36	3.00	2.78	2.47	–	3.16
Change (%)	0	+2	−9	−15	−25		−4
PD_{20} (mg)	0.50						

Technical comments: Test performance was good.
Test preparation requirements met.

Cautionary statements: The test quality is good.
Technical interpretation: Baseline ventilatory function is within normal limits. The response to inhaled methacholine is positive.
Clinical context: Results suggest AHR which is a feature of asthma. However, a positive finding is not specific for asthma, and other causes such as lung injury due to recent chest infection or smoking should also be considered.

Final Report: The test quality is good. Baseline ventilatory function is within normal limits. The response to inhaled methacholine is positive, suggesting AHR. Asthma and other causes, such as lung injury due to recent chest infection or smoking, should be considered in the light of other clinical findings.
Commentary: Saline is used as the diluent in methacholine solutions. Many methacholine protocols use a diluent inhalation step to assist with learning inhalation technique and to ensure that subjects are not sensitive to the diluent itself (see Table 6.2), though opinion is divided on whether a diluent step is required (4). Where a diluent step is used, change in FEV_1 throughout the challenge is calculated from the FEV_1 following the diluent (saline) dose.
Bronchodilator is provided to subjects with positive bronchial provocation test results and in some centres to each subject post-bronchial provocation test. The

bronchodilator response is compared to the diluent/placebo dose where one is delivered and to the baseline spirometry result where no placebo dose is administered. The primary reason for administering bronchodilator following bronchial provocation tests is for safety, ensuring that FEV_1 returns to within 10% of baseline FEV_1.

Case 2

Gender:	Female		
Age (yr):	41	Weight (kg):	81
Height (cm):	169	Race:	Caucasian
Clinical notes:	Chronic cough. ?asthma		

	Normal range	Baseline	*z*-score
Spirometry			
FEV_1 (L)	>2.61	3.66	1.09
FVC (L)	>3.25	4.61	1.34
FEV_1/FVC (%)	>72	79	−0.49

Challenge: Methacholine (dosimeter)

Dose (mg)	Saline	0.016	0.063	0.250	1.0	2.0	Post-BD
FEV_1 (L)	3.58	3.65	3.57	3.52	3.38	3.21	3.85
Change (%)	0	+2	0	−2	−6	−10	+8
PD_{20} (mg)	>2.0						

Technical comments: Test performance was good.
Test preparation requirements met.

Cautionary statements: The test quality is good.
Technical interpretation: Baseline ventilatory function is within normal limits. The response to inhaled methacholine is negative.
Clinical context: No evidence of AHR identified. Asthma is unlikely, though exercise-induced asthma cannot be excluded.

Final report: The test quality is good. Baseline ventilatory function is within normal limits. The response to inhaled methacholine is negative. No evidence of AHR identified. Asthma is unlikely, though exercise-induced asthma cannot be excluded. Clinical correlation is required.
Commentary: The maximum dose/concentration delivered with a methacholine challenge may vary depending on the protocol used in your laboratory. The protocol used in this example (7) uses a maximum dose of 2.0 mg methacholine delivered via a dosimeter. Note that the PD_{20} is written as >2.0 mg (which was the maximum dose delivered), rather than extrapolating using the dose–response curve (4).

Considering the clinical notes of this case, some may say that the addition of the final portion of the last sentence adds confusion to the report. The clinical notes are 'chronic cough, ?asthma'. The negative result suggests that asthma is unlikely (methacholine is a good rule-out test). However, the literature has shown that methacholine has low sensitivity for identifying exercise-induced asthma (15). The final sentence alerts the referring physician to consider if symptoms are worse on exertion and if further investigation is perhaps required.

Case 3

Gender:	Female	Date:	13/1/2013
Age (yr):	31	Weight (kg):	69
Height (cm):	172	Race:	Caucasian

Clinical notes: Hx of childhood asthma. ?current asthma. Nil ICSs.

	Normal range	Baseline	*z*-score
Spirometry			
FEV_1 (L)	>2.88	3.64	0.26
FVC (L)	>3.47	4.45	0.45
FEV_1/FVC (%)	>74	82	−0.41

Challenge: Hypertonic saline (4.5%)

Dose (mL)	1.2	2.6	6	12.9	19.8	Post-BD
FEV_1 (L)	3.48	3.43	3.30	3.23	3.09	3.49
Change (%)	−4	−6	−9	−11	−15	−4
PD_{15} (mL)	19.6					

Technical comments: Test performance was good.
Test preparation requirements met.

Cautionary statements: The test quality is good.
Technical interpretation: Baseline ventilatory function is within normal limits. The response to inhaled hypertonic saline is positive.
Clinical context: Results are suggestive of asthma with active airway inflammation.

Final report: The test quality is good. Baseline ventilatory function is within normal limits. The response to inhaled hypertonic saline is positive. Results are consistent with asthma with active airway inflammation.
Commentary: The volume of hypertonic saline delivered to the airways for each step is dependent on the output of the ultrasonic nebuliser and the respiratory pattern of the subject. Thus, the dose delivered at each step will be different for each subject. The dose for each step is calculated post-challenge by dividing the total weight loss from the nebuliser chamber by total inhalation time (5). This figure is then multiplied by the cumulative inhalation time for each step.

Case 4

Gender:	Female	Date:	18/4/2013
Age (yr):	31	Weight (kg):	69
Height (cm):	172	Race:	Caucasian

Clinical notes: Asthma. Previous positive saline challenge. Now using ICS.

	Normal range	Baseline	*z*-score
Spirometry			
FEV_1 (L)	>2.88	3.66	0.31
FVC (L)	>3.47	4.41	0.36
FEV_1/FVC (%)	>74	83	−0.21

Challenge:	Hypertonic saline (4.5%)					
Dose (mL)	0.79	2.37	5.53	11.85	24.5	Post-BD
FEV_1 (L)	3.55	3.51	3.53	3.52	3.39	3.62
Change (%)	−3	−4	−4	−4	−7	−1
PD_{15} (mL)	>24.5					

Technical comments: Test performance was good.
Test preparation requirements met.

Cautionary statements: The test quality is good.
Technical interpretation: Baseline ventilatory function is within normal limits. The response to inhaled hypertonic saline is negative.
Clinical context: Results are suggestive of asthma with controlled airway inflammation. In comparison with a previous hypertonic saline challenge on 13/1/2013 (see Case 3), there has been a significant reduction in AHR.

Final report: The test quality is good. Baseline ventilatory function is within normal limits. The response to inhaled hypertonic saline is negative, suggesting asthma with controlled airway inflammation on current therapy, though clinical correlation is required. In comparison with a previous hypertonic saline challenge on 13/1/2013, there has been a significant reduction in AHR.
Commentary: The subject in this case is the same subject as in Case 3. The subject returned for repeat testing 3 months after starting on ICSs and now appears to have better asthma control (reduced airway inflammation), though clinical correlation is required.

Case 5

Gender:	Male		
Age (yr):	21	Weight (kg):	80
Height (cm):	159	Race:	Caucasian

Clinical notes: ?Asthma

	Normal range	Baseline	*z*-score
Spirometry			
FEV_1 (L)	>3.14	4.48	1.86
FVC (L)	>3.67	5.35	2.07
FEV_1/FVC (%)	>74	84	0

Challenge:	Hypertonic saline (4.5%)					
Dose (mL)	0.5	1.6	3.7	7.9	16.3	Post-BD
FEV1 (L)	4.43	4.30	4.18	4.03	3.98	4.47
Change (%)	−1	−4	−7	−10	−10	0
PD_{15} (mL)	>16.3					
Technical comments:	Test performance was good. Less than 23.5 mL saline delivered. Incomplete test. Test preparation requirements met.					

Cautionary statements:	The test quality is good. However, suboptimal volume of saline was delivered to airway during challenge.
Technical interpretation:	Baseline ventilatory function is within normal limits. The response to inhaled hypertonic saline is inconclusive.
Clinical context:	Asthma cannot be excluded.

Final report: The test performance was good but the test was incomplete as a suboptimal volume of saline was delivered to the airway. Baseline ventilatory function is within normal limits. The response to inhaled hypertonic saline is inconclusive and asthma cannot be excluded. Consider repeat testing if still clinically indicated.
Commentary: Usually, sufficient hypertonic saline can be delivered to the airways in five doubling, stepped doses (30 s, 1 min, 2 min, 4 min and 8 min exposure). In this case, insufficient volume has been delivered to the airway in five doses and a sixth dose (8 min exposure) should have been delivered. Thus, the result is inconclusive. The reason for insufficient volume being delivered may be due to the subject's respiratory rate and/or tidal volume, or the nebuliser output being too low.

Case 6

Gender:	Female		
Age (yr):	30	Weight (kg):	87.5
Height (cm):	170	Race:	Caucasian
Clinical notes:	Diving medical. Obstruction on baseline spirometry. History of atopic asthma as a child.		

	Normal range	Baseline	*z*-score
Spirometry			
FEV_1 (L)	>2.83	2.16	−3.38
FVC (L)	>3.39	4.07	−0.16
FEV_1/FVC (%)	>75	53	−5.27

Challenge:	Mannitol									
Dose (mg)	0	5	15	35	75	155	315	475	635	Post-BD
FEV_1 (L)	2.09	2.02	1.90	1.87	1.82	1.71	–	–	–	2.31
Change (%)	0	−3	−9	−11	−13	−18				+11
PD_{15} (mg)	100									

Technical comments: Test performance was good. Note: Obstruction on baseline spirometry.
Test preparation requirements met.

Cautionary statements: The test quality is good.
Technical interpretation: Baseline ventilatory function reveals an obstructive ventilatory defect. The response to inhaled mannitol is positive.
Clinical context: Results suggest asthma with current airway inflammation.

Final report: The test performance was good. Baseline ventilatory function reveals an obstructive ventilatory defect. The response to inhaled mannitol is positive, suggesting asthma with current airway inflammation.
Commentary: The change in FEV_1 during a mannitol challenge is calculated from the 0 mg dose FEV_1, rather than the baseline FEV_1.

Case 7

Gender:	Male		
Age (yr):	49	Weight (kg):	91
Height (cm):	159	Race:	Caucasian

Clinical notes: Nocturnal cough, wheeze on exertion, particularly cold weather. ?Asthma.

	Normal range	Baseline	*z*-score
Spirometry			
FEV_1 (L)	>2.44	2.61	−1.19
FVC (L)	>3.16	3.20	−1.56
FEV_1/FVC (%)	>68	82	0.62

Challenge:	Mannitol									
Dose (mg)	0	5	15	35	75	155	315	475	635	Post-BD
FEV_1 (L)	2.70	2.70	2.71	2.67	2.53	2.59	2.69	2.51	2.64	2.74
Change (%)	0	0	0	−1	−6	−4	0	−7	2	+1
PD_{15} (mg)	>635									

Technical comments: Test preparation requirements met. Test performance was good.

Cautionary statements:	The test quality is good.
Technical interpretation:	Baseline ventilatory function is within normal limits. The response to inhaled mannitol is negative.
Clinical context:	Asthma cannot be excluded, consider further investigation if clinically indicated or an alternate diagnosis.

Final report: The test performance was good. Baseline ventilatory function is within normal limits. The response to inhaled mannitol is negative. Asthma cannot be excluded – consider further investigation if clinically indicated, or an alternate diagnosis.

Commentary: This case illustrates a negative mannitol challenge when the clinical history has a high probability of asthma. The mannitol challenge has low sensitivity so it is not a rule-out test – therefore, the subject may have asthma, it just has not been demonstrated on this occasion. The referring physician needs to consider the likelihood of asthma in the light of the clinical information and perhaps undertake further investigations or consider alternate diagnoses. Similar to methacholine challenges, the PD_{15} for a negative mannitol challenge is quoted as >635 mg, rather than extrapolating the results.

Case 8

Gender:	Female		
Age (yr):	31	Weight (kg):	57
Height (cm):	165	Race:	Caucasian

Clinical notes: ?asthma, wheeze on exertion.

	Normal range	Baseline	*z*-score
Spirometry			
FEV_1 (L)	>2.66	2.90	−1.00
FVC (L)	>3.18	3.54	−0.81
FEV_1/FVC (%)	>74	82	−0.39

Challenge: Mannitol

Dose (mg)	0	5	15	35	75	155	315	475	635	Post-BD
FEV_1 (L)	2.92	2.85	2.87	2.86	2.55	–	–	–	–	2.86
Change	0	−2	−2	−2	−13					−2
PD_{15} (mg)	85									

Technical comments: Test preparation requirements met. Test performance was good. Challenge terminated due to 10% fall in FEV_1 between consecutive doses.

Cautionary statements: The test quality is good.
Technical interpretation: Baseline ventilatory function is within normal limits. The response to inhaled mannitol is positive due to a 10% fall in FEV1 between consecutive doses.
Clinical context: Results suggest asthma with current airway inflammation.

Final report: The test performance was good. Baseline ventilatory function is within normal limits. The response to inhaled mannitol is positive. Results suggest asthma with current airway inflammation.
Commentary: At first glance, this challenge appears to be incomplete; however, mannitol challenges are considered positive if there is either a ≥15% fall in FEV_1 from 0 mg dose or a ≥10% fall in FEV_1 between consecutive doses (11). In this case, the fall between the 35 and 75 mg cumulative doses is 12%, hence meeting the criteria for a positive challenge. The PD_{15} can be extrapolated from the last two doses (11). (Note: Extrapolation for PD_{15} should only be calculated where there has been a 10% fall between doses and should not be performed if the full challenge has been performed with a negative result.)

Case 9

Gender:	Female		
Age (yr):	45	Weight (kg):	54
Height (cm):	165.5	Race:	Caucasian

Clinical notes: ?Exercise-associated asthma.

	Normal range	Baseline	*z*-score
Spirometry			
FEV_1 (L)	>2.42	3.26	0.63
FVC (L)	>3.05	4.22	1.03
FEV_1/FVC (%)	>71	77	–0.67

Challenge:	EVH						
Post-challenge (min)	1	3	5	7	10	15	Post-BD
FEV_1 (L)	–	1.85	–	–	–	–	2.98
Change (%)		–43					–9
Target ventilation:	97 L/min	Actual ventilation:			80 L/min		
Technical comments:		Test performance was good. Test preparation requirements met. Unable to obtain an FEV_1 at 1 min post-challenge due to cough. 600 μg salbutamol required to return spirometry to within 10% of baseline values.					

Cautionary statements: The test quality is good.
Technical interpretation: Baseline ventilatory function is within normal limits. The response to eucapnic voluntary hyperventilation is positive.
Clinical context: Results suggestive of current exercise-induced asthma.

Final report: The test performance was good. Baseline ventilatory function is within normal limits. The response to eucapnic voluntary hyperventilation is positive, suggesting current exercise-induced asthma.
Commentary: Note the large fall in FEV_1 at 3 min post-challenge (43%). A large fall in FEV_1 is a risk associated with single step/dose challenges. Note also that the subject failed to meet the target ventilation, but this was probably due to bronchoconstriction and as the result was positive, this is not of concern.

Case 10

Gender:	Female		
Age (yr):	31	Weight (kg):	72
Height (cm):	166	Race:	Caucasian

Clinical notes: Runs. Is exercise an asthma trigger?

	Normal range	Baseline	*z*-score
Spirometry			
FEV_1 (L)	>2.69	3.60	0.80
FVC (L)	>3.22	4.32	0.87
FEV_1/FVC (%)	>74	83	−0.15

Challenge:	EVH						
Post-challenge (min)	1	3	5	7	10	15	Post-BD
FEV_1 (L)	3.40	3.41	3.34	3.38	3.41	3.39	3.46
Change (%)	−6	−5	−7	−6	−5	−6	−4
Target ventilation:	107 L/min	Actual ventilation:			94 L/min		
Technical comments:		Test preparation requirements met. Test performance was fair. Unable to achieve target ventilation.					

Cautionary statements: The test quality is fair – target ventilation not achieved.
Technical interpretation: Baseline ventilatory function is within normal limits. The response to eucapnic voluntary hyperventilation is inconclusive as target ventilation was not achieved.
Clinical context: Exercise-induced asthma cannot be excluded.

Final report: The test performance was fair as target ventilation not achieved. Baseline ventilatory function is within normal limits. The response to eucapnic voluntary hyperventilation is inconclusive as target ventilation was not achieved. Exercise-induced asthma cannot be excluded.
Commentary: Note that the target ventilation is not achieved and in the absence of significant change in FEV_1, this test is inconclusive. The airways may not have been dried sufficiently through ventilation to trigger the inflammatory cascade leading to bronchoconstriction.

Case 11

Gender:	Female		
Age (yr):	22	Weight (kg):	64.4
Height (cm):	160.3	Race:	Caucasian
Clinical notes:	National-level hockey. ?exercise-associated asthma		

	Normal range	Baseline	*z*-score
Spirometry			
FEV_1 (L)	>2.65	2.95	−0.76
FVC (L)	>3.00	3.73	+0.13
FEV_1/FVC (%)	>76	79	−1.18

Challenge:	EVH						
Post−challenge (min)	1	3	5	7	10	15	Post-BD
FEV_1 (L)	2.88	2.77	2.86	2.89	2.86	2.89	3.08
Change (%)	−2	−6	−3	−2	−3	−2	+4
Target ventilation:	88 L/min	Actual ventilation:			98 L/min		
Technical comments:		Test performance was good. Target ventilation achieved. Test preparation requirements met. Not using ICSs.					

Cautionary statements:	The test quality is good.
Technical interpretation:	Baseline ventilatory function is within normal limits. The response to eucapnic voluntary hyperventilation is negative.
Clinical context:	Exercise-induced asthma cannot be excluded.

Final report: The test performance was good. Baseline ventilatory function is within normal limits. The response to eucapnic voluntary hyperventilation is negative. Results cannot exclude exercise-induced asthma – consider other investigations based on clinical indications or consider alternate diagnoses.

Commentary: The EVH test in a clinical population has low sensitivity and hence a negative result cannot exclude exercise-induced asthma in such a population (12). There is some evidence, however, that the sensitivity for EVH to detect bronchoconstriction is higher in elite athletes (16), into which category this subject probably fits.

Consideration could be given to referring the patient for a direct challenge test such as methacholine (keeping in mind that methacholine also has a low sensitivity for exercise-induced asthma). If that test is also negative, then the likelihood of asthma is small. However, if the direct challenge test is positive, this leads to the unfortunate situation (from a clinical perspective) where a positive direct challenge test is equally as unhelpful (not specific for asthma) as a negative indirect challenge.

References

1 Joos GF, O'Connor B, Anderson SD, Chung F, Cockcroft DW, Dahlen B, et al. Indirect airway challenges. Eur Respir J. 2003 Jun; 21(6):1050–68.
2 Cockcroft DW. Direct challenge tests: Airway hyperresponsiveness in asthma: its measurement and clinical significance. Chest. 2010 Aug; 138(2 Suppl):18S–24S.
3 Anderson SD. Indirect challenge tests: airway hyperresponsiveness in asthma: its measurement and clinical significance. Chest. 2010 Aug; 138(2 Suppl):25S-30S.
4 Crapo RO, Casaburi R, Coates AL, Enright PL, Hankinson JL, Irvin CG, et al. Guidelines for methacholine and exercise challenge testing-1999. This official statement of the American Thoracic Society was adopted by the ATS Board of Directors, July 1999. Am J Respir Crit Care Med. 2000 Jan; 161(1):309–29.
5 Anderson SD, Brannan JD. Methods for "indirect" challenge tests including exercise, eucapnic voluntary hyperpnea, and hypertonic aerosols. Clin Rev Allergy Immunol. 2003 Feb; 24(1):27–54.
6 Argyros GJ, Roach JM, Hurwitz KM, Eliasson AH, Phillips YY. Eucapnic voluntary hyperventilation as a bronchoprovocation technique: development of a standarized dosing schedule in asthmatics. Chest. 1996 Jun; 109(6):1520–4.
7 Chinn S, Burney P, Jarvis D, Luczynska C. Variation in bronchial responsiveness in the European Community Respiratory Health Survey (ECRHS). Eur Respir J. 1997 Nov; 10(11):2495–501.
8 Yan K, Salome C, Woolcock AJ. Rapid method for measurement of bronchial responsiveness. Thorax. 1983 Oct; 38(10):760–5.
9 Cockcroft DW, Davis BE. Diagnostic and therapeutic value of airway challenges in asthma. Curr Allergy Asthma Rep. 2009 May; 9(3):247-53.
10 Busse WW. What is the best pulmonary diagnostic approach for wheezing patients with normal spirometry? Respir Care. 2012 Jan; 57(1):39-46; discussion 7–9.
11 Brannan JD, Anderson SD, Perry CP, Freed-Martens R, Lassig AR, Charlton B. The safety and efficacy of inhaled dry powder mannitol as a bronchial provocation test for airway hyperresponsiveness: a phase 3 comparison study with hypertonic (4.5%) saline. Respir Res. 2005; 6:144.
12 Eliasson AH, Phillips YY, Rajagopal KR, Howard RS. Sensitivity and specificity of bronchial provocation testing. An evaluation of four techniques in exercise-induced bronchospasm. Chest. 1992 Aug; 102(2):347–55.
13 Hurwitz KM, Argyros GJ, Roach JM, Eliasson AH, Phillips YY. Interpretation of eucapnic voluntary hyperventilation in the diagnosis of asthma. Chest. 1995 Nov; 108(5):1240–5.
14 Anderson SD, Brannan J, Spring J, Spalding N, Rodwell LT, Chan K, et al. A new method for bronchial-provocation testing in asthmatic subjects using a dry powder of mannitol. Am J Respir Crit Care Med. 1997 Sep; 156(3 Pt 1):758–65.
15 Anderson SD. Provocative challenges to help diagnose and monitor asthma: exercise, methacholine, adenosine, and mannitol. Curr Opin Pulm Med. 2008 Jan; 14(1):39–45.
16 Holzer K, Anderson SD, Douglass J. Exercise in elite summer athletes: challenges for diagnosis. J Allergy Clin Immunol. 2002 Sep; 110(3):374–80.

CHAPTER 7

The importance of quality tests

Assessment of test quality is an essential step in the interpretation strategy. A suboptimal quality result reported as a good quality result may result in misclassification and incorrect management of a patient. Some might say a lung function test that has been done poorly is worse than not having the test done at all.

Test quality may be impacted by patient-related factors and/or equipment-related/technical factors (Table 7.1).

Assessment of test quality depends on the following:

- Ability and skills of test operator
- Accurate technical comments regarding test quality from test operator
- Reporter's knowledge of the principles of test measurement
- Reporter's knowledge of the impact of suboptimal quality test on interpretation of results

The test operator's role in test quality includes the following:

- Ensuring the equipment is calibrated and performing within its specifications
- Having a sound knowledge of the test methodologies and the within-test acceptability and repeatability criteria
- Providing instruction to the subject to elicit maximal effort, inspecting the raw data for acceptability and repeatability criteria and providing feedback to the subject to maximise test quality
- Knowledge of between-test quality indicators
- Documenting the test quality and specific factors that may affect test quality, often referred to as a technical comment. To promote consistency between test operators, some laboratories use quality rating scales (Table 7.2) (1, 2).

Interpreting Lung Function Tests: A Step-by-Step Guide, First Edition.
Brigitte M. Borg, Bruce R. Thompson and Robyn E. O'Hehir.
© 2014 John Wiley & Sons, Ltd. Published 2014 by John Wiley & Sons, Ltd.

Table 7.1 Examples of factors that affect test quality.

Patient related	*Equipment/technical related*
Patient cooperation	Lack of calibration
Patient coordination	Incorrect ambient conditions entered
Patient cognition	Poor linearity of analysers/flow sensors
Patient effort	Inaccurate/imprecise devices
Language barriers	Drift
Pain	Leak
Inability to meet test acceptability criteria Inability to meet test repeatability criteria	Operator-related issues • Lack of knowledge of acceptability and repeatability criteria • Unable to elicit a maximal effort from subject • Poor attention to detail with respect to inspection of individual efforts • Poor feedback provided to patients on how to improve test quality

Table 7.2 An example of a spirometry quality rating scale (1,2).

Rating	*Description*	*Interpretation*
Good	3 acceptable efforts AND, of these acceptable efforts: • Best two FEV_1s match to within 150 mL AND • Best two FVCs match to within 150 mL	Good representation of the patient's true lung function
Fairly good	2 acceptable efforts AND, of these acceptable efforts: • Best two FEV_1s match to within 150 mL AND • Best two FVCs match to within 150 mL	Fairly good representation of the patient's true lung function
Fair	≥2 acceptable efforts AND, of these acceptable efforts: • Best two FEV_1s are not within 150 mL OR • Best two FVCs are not within 150 mL	Fair representation of the patient's true lung function – interpret using some caution
Fairly poor	Only one acceptable test	Use caution in interpretation of the results – not satisfied that results are representative of the patient's true lung function
Poor	No acceptable tests	Interpretation of the results is probably not possible, but may be able to say, for example, 'VC is at least … '

The reporter's role in assessment of test quality includes the following:

- Inspection of raw data and/or inspection of technical comments
- Understanding the principles of measurement
- Understanding the within-test quality factors (see test-specific chapters for details)
- Knowledge of between-test quality indicators
  Some simple between-test indicators of good quality (spirometry, T_LCO, static lung volumes) include the following:
  — The inspiratory vital capacity (IVC) (from T_LCO) should be within 85% of the maximum vital capacity (VC) measured. If IVC < 85% of maximum VC, this may impact on V_A and T_LCO (see Case 5).
  — The slow vital capacity (SVC) measured as part of static lung volumes (total lung capacity (TLC)-residual volume (RV)) should be greater than FVC-150 mL. This is a check of repeatability – that the SVC and the FVC are similar. In individuals with significant airflow limitation, SVC ≫ FVC, but it is unusual for FVC ≫ SVC, and when seen, this often reflects suboptimal test performance or technical issues (see Case 4).
  — The TLC-RV should be greater than V_I (from T_LCO)-150 mL. As for the point earlier, this is a check of repeatability.
  — The TLC should be greater than V_A (from T_LCO), especially in patients with airflow obstruction. Because of differences between devices and test methodologies, V_A may occasionally be just larger than TLC. However, if V_A is markedly higher than TLC, test performance or technical issues should be considered.
- Identifying the impact of suboptimal quality tests on interpretation of results in the report.

To report or not to report suboptimal quality tests?

Although tests of good quality are said to provide a good representation of a patient's true lung function, tests of suboptimal quality may not.

Sometimes, no test results are better than providing suboptimal test results that may lead to misclassification. However, some aspects of a suboptimal quality result may provide useful information that is worth reporting.

For example: A patient with cognitive impairment has difficulties producing maximal expiratory efforts during a spirometry test. The patient is unable to blow fast, but seems to be blowing from TLC to RV. As the patient is not blowing maximally, the FEV_1 reported is unlikely to be a true FEV_1 (as the manoeuvre is not forced), so it should not be reported. However, the total volume exhaled indicates that the VC is at least a certain amount.

If considering using tests of suboptimal quality, then consider the following:

- The risk of misclassification
- The impact of the quality on the interpretation

Use cautionary statements in the report to make it clear to the reader that there is an issue that may impact the interpretation. If you are able to determine the size and direction of the impact, then this should also be noted.

Examples of assessment of test quality

Steps in assessing test quality:

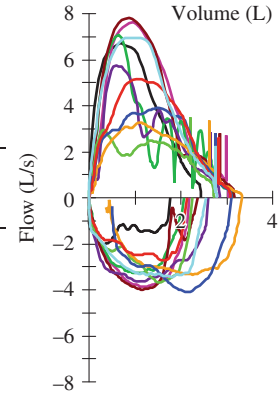
- Read technical comment
- Perform the simple between-test assessments of quality described earlier
- Inspect raw data if able or where necessary
- Evaluate impact of suboptimal quality on interpretation of results
- Include a statement regarding test quality in the report based on the evidence
- Where suboptimal quality is present – the statement should be cautionary and describe the impact of the issue on the interpretation of results.

Case 1

Gender:	Male		
Age (yr):	68	Weight (kg):	73.5
Height (cm):	169	Race:	Caucasian

Clinical notes: Lung mass. Baseline spirometry please.

	Normal range	Baseline	*z*-score
Spirometry			
FEV_1 (L)	>2.19	2.99	+0.21
FVC (L)	>3.09	3.04	−1.74
VC (L)	>3.09	3.33	−1.17
FEV_1/(F)VC (%)	>64	90	+2.68



Technical comment: Test performance was fairly poor. Poor technique, glottic interference, tongue occluding mouthpiece, back extrapolation error. FVC likely to be underestimated. FEV_1 may be impacted.

Cautionary statements: Results should be interpreted with caution as test performance was fairly poor with FEV_1 and FVC likely to be underestimated.

Technical interpretation: Despite the fairly poor test performance, baseline spirometry appears to be within normal limits.

Clinical context:

Final report: Results should be interpreted with caution as test performance was fairly poor with FEV_1, and FVC was likely to be underestimated. Despite this, baseline spirometry appears to be within normal limits.

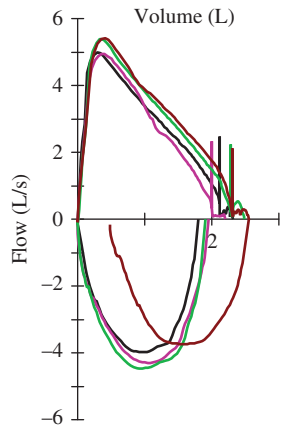
Commentary: The superimposed flow–volume loops show the lack of acceptability and repeatability of the results. Some efforts lack maximal effort; others appear to have artefact related to tongue occluding the mouthpiece and glottic interference with early termination. There is concern about whether the FEV_1 is accurate, and the FVC is probably underestimated. The VC from an effort with a submaximal start provides the largest VC value and has been quoted as such. Although we are unable to be certain that the results are an accurate reflection of the patient's true lung function, the results appear to be within normal limits and this is useful information for the referring physician. It should also be noted that no clinical context is provided in this case due to the uncertainty in the results.

Case 2

Gender:	Female		
Age (yr):	20	Weight (kg):	65.8
Height (cm):	157.5	Race:	Caucasian
Clinical notes:	Asthma.		

	Normal range	Baseline	*z*-score	Post-bronchodilator (BD)	Change (%)
Spirometry					
FEV_1 (L)	>2.59				
FVC (L)	>2.89				
VC (L)	>2.89	2.55	–2.51	2.53	–2.56
FEV_1/(F)VC (%)	>77				

Technical comment: Test performance was fairly poor. Good start, glottic interference on all efforts impacting FEV_1 and FVC. FEV_1 likely to be underestimated. VC quoted is best of FVCs, but likely to be underestimated. Post-bronchodilator test performance similar.



Cautionary statements: Results should be interpreted with caution as test performance was fairly poor. FEV_1 and FVC not quoted as likely to have been impacted by glottic interference (underestimated). Post-bronchodilator spirometry had similar pattern.

Technical interpretation: The VC appears to be reduced; however, this may be underestimated due to test performance. The loop shape does not appear to show evidence of obstruction.

Clinical context:

Final report: Results should be interpreted with caution as test performance was fairly poor. FEV_1 and FVC not quoted as they are likely to have been underestimated due to glottic interference. The VC appears to be reduced; however, this may be underestimated due to test performance. Static lung volumes may assist with confirming restriction. The loop shape does not appear to show evidence of obstruction.

Commentary: The flow volume loops shown here represent the baseline efforts. Although the beginning of each effort meets start of test acceptability criteria, glottic interference leads to a disruption to airflow and affects FEV_1 and probably FVC. The best FVC has been quoted as the VC, as this provides some information. The shape of the flow volume curve does not suggest airflow limitation related to asthma, though there is obstruction related to glottic interference. It is difficult to provide a clinical context when test performance is submaximal.

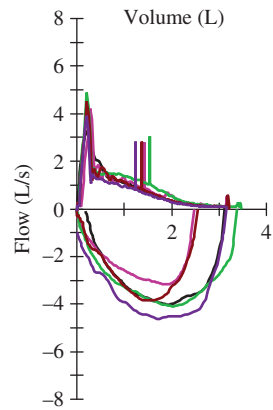
Case 3

Gender:	Male		
Age (yr):	60	Weight (kg):	78.8
Height (cm):	173.5	Race:	Caucasian

Clinical notes: Chronic cough. ?COPD

	Normal range	Baseline	*z*-score	Post-BD	Change (%)
Spirometry					
FEV_1 (L)	>2.65	1.55	−4.05	1.70	+10
FVC (L)	>3.60	3.47	−1.89	3.64	+5
FEV_1/(F)VC (%)	>66	45	−5.27	47	

Technical comment: Test performance was fair. Baseline FVC not repeatable – patient complained of chest tightness. Post-bronchodilator values repeatable.



Cautionary statements: Results should be interpreted with caution as baseline FVC is not repeatable, though this would not necessarily impact on overall results. Chest tightness noted by patient during baseline tests.

Technical interpretation: There is an obstructive ventilatory defect with a reduced FVC. The response to inhaled bronchodilator is not significant, but returns FVC to within the normal range, suggesting FVC is possibly reduced due to airflow limitation. Static lung volumes could be performed to further elucidate results.

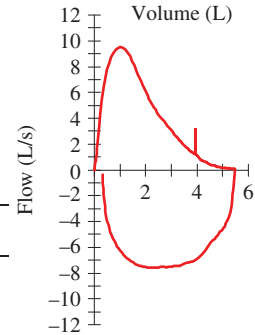
Clinical context: Results are consistent with the spirometric definition of COPD.

Final report: Results should be interpreted with caution as baseline FVC is not repeatable, although the impact on overall results is likely to be small. There appears to be an obstructive ventilatory defect with a reduced FVC. The response to inhaled bronchodilator is not significant, but returns FVC to within the normal range, suggesting FVC is probably reduced due to airflow limitation. Static lung volumes could be performed to further elucidate results. Results are consistent with the spirometric definition of COPD.

Commentary: The flow volume loops shown here represent the baseline efforts. Although the baseline FVC is not repeatable, that is, the highest and second highest FVC from acceptable baseline efforts are more than 150 mL apart, the impact on the overall results is likely to be small. There was no significant increase in FVC with bronchodilator (though results come to within normal limits) and post-bronchodilator FVC results are repeatable, suggesting that the highest recorded FVC from baseline efforts was probably a close reflection of true lung function. Results with poor repeatability should not be excluded from reports and interpretation (3), but the person undertaking the interpretation needs to determine the impact of the lack of repeatability.

Case 4

Gender:	Male		
Age (yr):	45	Weight (kg):	75.5
Height (cm):	181	Race:	Caucasian
Clinical notes:	Reduced exercise tolerance, chronic cough. Smoking history of 10 pack years – ceased at 40 years.		



	Normal range	Baseline	*z*-score
Spirometry			
FEV_1 (L)	>3.42	3.96	−0.56
FVC (L)	>4.43	5.47	+0.12
FEV_1/FVC (%)	>69	72	−1.08
Static lung volumes			
TLC (L)	5.90–8.50		
RV (L)	<2.61		
FRC (L)	2.48–4.84	4.79	+1.58
RV/TLC (%)	<35		
VC (L)	>4.43		
Single breath carbon monoxide transfer factor			
V_I (L)		5.08	
V_A (L)	>6.5	7.5	−0.12
T_LCO (mmol/min/kPa)	>8.4	9.3	−0.93
$T_LCO_{Hb\ corr}$ (mmol/min/kPa)		9.1	−1.06
KCO (mmol/min/kPa/L)	1.1–1.8	1.2	−1.09
$KCO_{Hb\ corr}$ (mmol/min/kPa/L)		1.2	−1.29
Hb (g/dL)		15.2	

Technical comment:	Test performance good for spirometry and gas transfer. For static lung volumes, SVC ≪ FVC – trouble with performing SVC manoeuvre.

Individual results for static lung volume measurements are as follows:
The test was performed using the preferred method for body plethysmography (after the FRC measurement the subject blows out to RV and then breathes in to TLC) (4).

Measured values					*Acceptability of test components*		*Used to calculate result*	*Calculated results*	
Trial	FRC (L)	ERV (L)	SVC (L)	Pant frequency (/min)	FRC	SVC		RV (L)	TLC (L)
1	5.02	0.34	1.48	103	× – pant frequency high	× – SVC ≪ FVC[a] – 150 mL			
2	4.90	1.36	4.13	46	✓	× – SVC ≪ FVC – 150 mL			
3	4.86	1.35	4.13	68	✓	× – SVC ≪ FVC – 150 mL			
4	4.78	1.69	3.16	68	✓	× – SVC ≪ FVC – 150 mL			
5	4.75	1.83	4.86	73	✓	× – SVC < FVC – 150 mL	✓		
6	4.84	2.00	5.08	71	✓	× – SVC < FVC – 150 mL	✓		
7	4.75	1.44	4.01	48	✓	× – SVC ≪ FVC – 150 mL			
Result	4.79	1.92	5.08	–				2.88	7.96

[a] FVC = 5.47 L

Cautionary statements:	Spirometry and gas transfer tests are of good quality. Static lung volume results are not of good quality due to SVC test performance and only FRC results are reported.
Technical interpretation:	Baseline ventilatory function is within normal limits. FRC is within normal range. Alveolar volume and carbon monoxide transfer factor, corrected for haemoglobin, are within normal limits.
Clinical context:	Cause of symptoms is not evident from results on this occasion.

Final report: Spirometry and gas transfer results are of good quality. Static lung volumes were not performed well and only FRC is reported. Baseline ventilatory function is within normal limits. Functional residual capacity is within normal limits. Alveolar volume and carbon monoxide transfer factor, corrected for haemoglobin, are within normal limits. The cause of the noted symptoms is not evident from these results on this occasion.
Commentary: In this case, the spirometry and TLCO measurements have been performed well and can be reported as good quality tests.

For static lung volumes, all FRC measurements meet acceptability and repeatability criteria except for one where the pant frequency is high; hence, an FRC result can be reported. The linked, SVC manoeuvres, however, were not performed well:

- For some efforts, it appears that the subject did not exhale completely to RV (ERV is variable) which will in turn affect the SVC. It is unclear whether the largest recorded ERV is maximal either.
- The SVCs measured are also variable: the largest SVC measured is 390 mL less than the largest recorded FVC (5.08 L versus 5.47 L). SVC may be reduced because the patient did not inhale maximally or because he did not blow out RV prior to SVC manoeuvre.

The possible impacts of these results include the following:

- RV may be overestimated if subject has not exhaled fully to true RV (ERV underestimated).
- TLC may be underestimated if subject has not breathed in sufficiently to TLC (SVC underestimated).
- A combination of both.

If the calculated RV and TLC (2.88 L and 7.96 L, respectively, see results earlier) were reported, the RV would appear to be elevated (>ULN), the TLC would be within normal limits and the RV/TLC would be just above the ULN. This causes confusion as this pattern is not expected when considered with the subject's baseline spirometry (no evidence of obstruction on spirometry – yet SLV results imply possible gas trapping or possible respiratory muscle dysfunction). Since the impact of the poorly performed SVC manoeuvre is not clear (is RV truly elevated or did the subject not exhale sufficiently?), only the FRC value is reported.

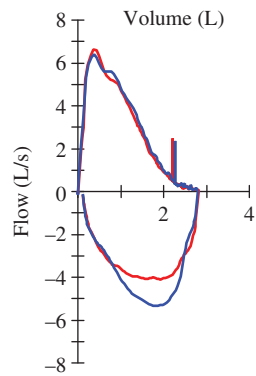
Case 5

Gender:	Female		
Age (yr):	48	Weight (kg):	49.3
Height (cm):	155	Race:	Caucasian

Clinical notes: Recent admission for pneumonia. Current smoker

	Normal range	Baseline	*z*-score	Post-BD	Change (%)
Spirometry					
FEV_1 (L)	>2.04	2.23	−1.07	2.28	+2
FVC (L)	>2.59	2.86	−0.94	2.80	−2
FEV_1/FVC (%)	>71	78	−0.44	81	
Single breath carbon monoxide transfer factor					
V_I (L)		2.13			
V_A (L)	>3.7	3.5	−2.07		
T_LCO (mmol/min/kPa)	>5.0	6.0	−0.51		
$T_LCO_{\text{Hb corr}}$ (mmol/min/kPa)		5.9	−0.70		
KCO (mmol/min/kPa/L)	1.0–1.8	1.7	+1.36		
$KCO_{\text{Hb corr}}$ (mmol/min/kPa/L)		1.7	+1.19		
Hb (g/dL)		14.4			

Technical comment: Test performance good for spirometry. Gas transfer: $V_I < 85\%$ FVC



(*continued*)

Previous results: Nil

Cautionary statements:	Spirometry test is of good quality. Gas transfer test is only fair quality – $V_I < 85\%$ FVC and may result in underestimation of V_A and $T_L CO$.
Technical interpretation:	Baseline ventilatory function is within normal limits. The response to inhaled bronchodilator is not significant. Alveolar volume is reduced and carbon monoxide transfer factor, corrected for haemoglobin, is within normal limits. The reduction in alveolar volume may be due to test performance.
Clinical context:	No previous results are available for comparison.

Final report: Spirometry test is of good quality. Gas transfer test is only fair quality and may result in underestimation of V_A and $T_L CO$. Baseline ventilatory function is within normal limits with no significant response to inhaled bronchodilator. Alveolar volume is reduced and carbon monoxide transfer factor, corrected for haemoglobin, is within normal limits. The reduction in alveolar volume may be due to test performance. No previous results are available for comparison.

Commentary:

$V_I < 85\%$ FVC may be due to the following (5, 6):

- Failure to maximally inhale from RV to TLC, resulting in underestimation of V_A and to a lesser extent $T_L CO$.
- Failure to exhale to RV prior to taking VC breath in, which is thought to have little effect on V_A or $T_L CO$.

The test operator is probably best placed to determine the reason for the small V_I at the time of testing. Review of the raw data may also provide clues as to which of the two reasons is more likely. This will be dependent on the testing device used and other measurements that were performed though.

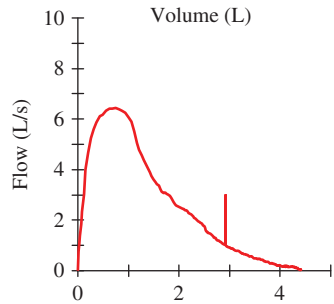
Case 6

Gender:	Male		
Age (yr):	65	Weight (kg):	61
Height (cm):	175.5	Race:	Caucasian

Clinical notes: Probable motor neuron disease. Respiratory muscle impairment?

	Normal range	Baseline	*z*-score	Supine	Change (%)
Spirometry					
FEV_1 (L)	>2.55	3.01	−0.67		
FVC (L)	>3.55	4.47	+0.03		
FEV_1/FVC (%)	>65	67	−1.24		
VC (L)	>3.55	4.45	+0.03	4.12	−7
Maximal respiratory pressures					
$P_I$max (cmH_2O)	>56	75	−0.76		
$P_E$max (cmH_2O)	>93	68	−3.12		

Technical comment: Test performance was fairly good for spirometry – PEF variable. Test performance was good for $P_I$max, but fairly poor for $P_E$max – difficulty maintaining mouth seal, results likely to be underestimated.



Cautionary statements: Results for maximal expiratory pressure should be interpreted with caution as mouth leak is likely to result in underestimation of results.

Technical interpretation: Baseline ventilatory function is within normal limits. The difference between upright and supine VC suggests no significant diaphragm weakness (<30% fall between upright and supine VC). The maximal inspiratory pressure is within normal limits. The maximal expiratory pressure is reduced; however, results may be underestimated due to leak during manoeuvres.

Clinical context: Significant inspiratory respiratory muscle impairment is unlikely, though expiratory muscle impairment cannot be ruled out.

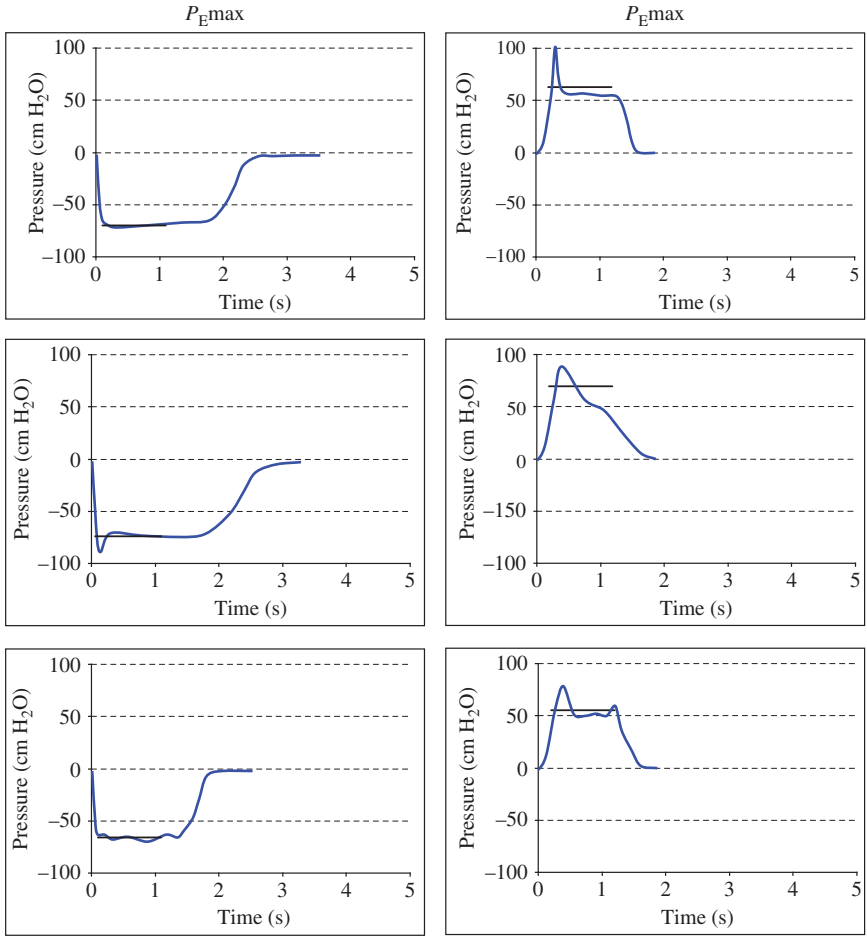


Figure 7.1 Pressure-time traces for best three maximal inspiratory and expiratory respiratory pressure efforts for Case 6.

Final report: Test quality is fairly good for spirometry – some variability in peak expiratory flow and good for maximal respiratory pressure. Leak during maximal expiratory pressure measurement is likely to result in underestimation of $P_E$max. Baseline ventilatory function is within normal limits. The difference between upright and supine VC suggests no significant diaphragm weakness. The maximal inspiratory pressure is within normal limits. The maximal expiratory pressure is reduced, though this is likely to be underestimated due to suboptimal test performance. Significant respiratory inspiratory muscle weakness is unlikely, though respiratory expiratory muscle weakness cannot be ruled out due to suboptimal test performance on this occasion.

Commentary: Figure 7.1 and Table 7.3 show the three best $P_I$max and $P_E$max efforts for this case. For $P_I$max, a sustained pressure for 1 s can be seen for all three

Table 7.3 Three best efforts for maximal inspiratory and expiratory respiratory pressures for Case 6.

Effort	$P_{I}max$ *(cm H_2O)*	$P_{E}max$ *(cm H_2O)*
1	70	60
2	75	68
3	67	54

efforts. The operator notes that the test was of good quality. For $P_E$max, there is difficulty sustaining the pressure for 1 s due to leak around the mouth. Leak renders the effort unacceptable (7), and consideration should be given to whether or not a result should be recorded for $P_E$max at all in this case? Leak generally results in underestimation of the sustained pressure. Therefore, in the report it needs to be clear that $P_E$max is likely to be underestimated. This is particularly important in this case as $P_E$max is below the lower limit of normal and could mislead clinical decision making.

Case 7

Gender:	Male		
Age (yr):	54	Weight (kg):	85.5
Height (cm):	185.4	Race:	Caucasian

Clinical notes: ?asthma

	Normal range	Baseline	*z*-score
Spirometry			
FEV_1 (L)	>3.34	3.62	−1.10
FVC (L)	>4.45	4.26	−1.96
FEV_1/FVC (%)	>67	85	+1.37

Challenge: Mannitol

Dose (mg)	0	5	15	35	75	155	315	475	635	Post-BD
FEV_1 (L)	3.46	3.42	3.25	3.10	3.36	3.01	3.04	2.77	–	3.40
Change (%)	0	−1	−6	−10	−3	−13	−12	−20		−2
PD_{15} (mg)	366									

Technical comment: Test performance was fair to poor. Variable inspiratory volumes. Baseline FVC likely to be underestimated. Difficulty getting repeatable FEV_1. ? true response.
Test preparation requirements met.

Cautionary statements: Results should be interpreted with caution as suboptimal quality spirometry may result in false-positive challenge result.

Technical interpretation: There appears to be a restrictive ventilatory defect on baseline spirometry, though this may be due in part to test performance. The response to inhaled mannitol challenge appears to be positive, though variability in test performance may contribute to results presented.

Clinical context: Current asthma is possible, though clinical correlation is required due to variable test performance.

Final report: Test quality is suboptimal and caution is required in interpreting results. There appears to be a restrictive defect on baseline spirometry, though FVC is likely to be underestimated due to suboptimal test performance. Static lung volumes are suggested to confirm restriction. The response to inhaled mannitol challenge appears to be positive, though the variable test performance may contribute to the positive result. Current asthma is possible, though clinical correlation is required due to the variable test performance.

Commentary: Interpretation of challenge results relies on spirometry being performed well. Because a fall in FEV_1 is the endpoint, if FEV_1 is variable due to test performance, uncertainty in interpretation of results can occur. Table 7.4 shows the FEV_1s measured at each stage of the challenge test for this case. Figure 7.2 shows the efforts from the cumulative 155 mg dose. Remember that timing to ensure cumulative effect is important in stepped challenge tests. Hence, two acceptable and repeatable FEV_1s within a stage are usually considered sufficient to move on to next dosing level. In this case, multiple efforts are required to get acceptable results for many stages of the challenge test and, for the 75 and 315 mg doses, repeatability is not achieved. The test operator indicates via the technical comments that the positive response may be a reflection of bronchoconstriction, poor test performance or a combination of both. The report needs to reflect this uncertainty. Some test operators may choose to terminate a bronchial provocation test if spirometry performance is variable because of the clinical uncertainty that may arise.

Table 7.4 FEV_1 values measured at each stage of the challenge test for Case 7.

		FEV_1 (L) *Mannitol dose (mg)*									
Stage	*Baseline*	*0*	*5*	*15*	*35*	*75*	*155*	*315*	*475*	*635*	*Post-BD*
Effort											
1	3.38	3.46	3.33	3.05	2.89	3.08[a]	2.51[a]	2.44[a]	2.85[a]	-	3.11[a]
2	3.27	3.30[a]	3.27	3.25	3.10	3.20	2.71[a]	2.51[a]	2.61[a]		3.38
3	3.21[a]	3.39	3.42	2.85[a]	2.96	3.10[a]	2.96	2.73	2.73		3.23
4	3.39[a]			2.98		3.36	2.87	3.04	2.02[a]		3.40
5	3.62			3.11		3.11[a]	3.01		2.77		
6	3.43[a]										
7	3.56										
8	3.34[a]										
Best	3.62	3.46	3.42	3.25	3.10	3.36	3.01	3.04	2.77	–	3.40

[a] Unacceptable efforts including incomplete inhalation to TLC, slow take-off, effort not forced or maximal, cough before 1 s.

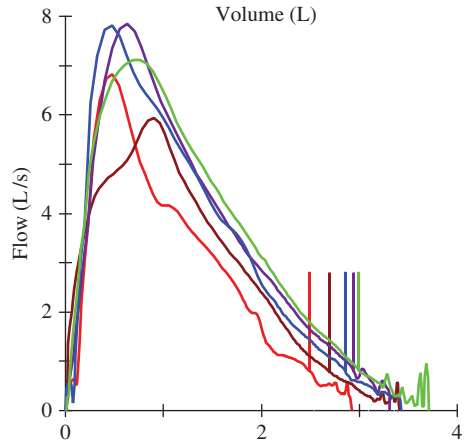
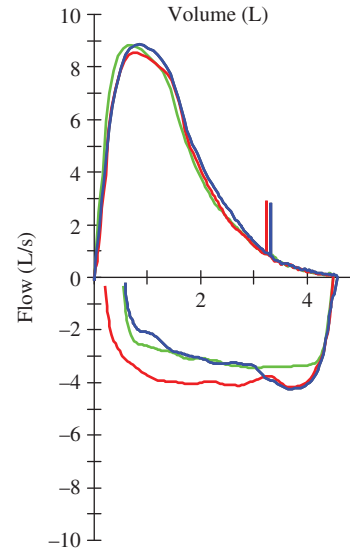


Figure 7.2 Variability in spirometry at cumulative 155 mg mannitol dose.

Case 8

Gender:	Male		
Age (yr):	53	Weight (kg):	55.6
Height (cm):	170.5	Race:	Caucasian
Clinical notes:	Recent pneumonia. Extensive smoking history. Changes on chest X-ray consistent with COPD.		



	Normal range	Baseline	*z*-score
Spirometry			
FEV_1 (L)	>2.75	3.34	−0.31
FVC (L)	>3.65	4.57	+0.13
FEV_1/FVC (%)	>67	73	−0.69
Single breath carbon monoxide transfer factor			
V_I (L)		4.14	
V_A (L)	>5.6	6.0	−1.01
T_LCO (mmol/min/kPa)	>7.0	3.7	−4.31
$T_LCO_{Hb\ corr}$ (mmol/min/kPa)		3.9	−4.20
KCO (mmol/min/kPa/L)	1.0–1.7	0.6	−4.32
$KCO_{Hb\ corr}$ (mmol/min/kPa/L)		0.6	−4.18
Hb (g/dL)		13.5	

Technical comment:	Spirometry test performance was fairly good, although inspiratory loops are submaximal. Test performance for T_LCO was good.

Previous results: Nil

Cautionary statements:	Test quality is good, excepting submaximal inspiratory loop during spirometry.
Technical interpretation:	Baseline ventilatory function is within normal limits. Inspiratory limb of the flow volume curve appears to be a little flattened, but this may be explained by submaximal inspiratory effort. Alveolar volume is within normal limits and carbon monoxide transfer factor, corrected for haemoglobin, is reduced, suggestive of parenchymal or pulmonary vascular disease.
Clinical context:	No previous results are available for comparison. Ventilatory function appears to be within normal limits, though there is evidence of gas exchange impairment.

Final report: The test is of good quality, excepting submaximal inspiratory effort during spirometry. Baseline ventilatory function is within normal limits. The inspiratory limb of the flow volume loop appears flattened, but this may be explained by submaximal inspiratory efforts. Alveolar volume is within normal limits and carbon monoxide transfer factor, corrected for haemoglobin, is reduced, suggestive of parenchymal or pulmonary vascular disease. Ventilatory function appears to be within normal limits, though there is evidence of gas exchange impairment.
Commentary: The overall quality of this test is good. The expiratory phase of spirometry is acceptable and repeatable. The carbon monoxide transfer factor test has also been performed well. The flattened inspiratory loops are, however, of concern. If no technical comments had been made, variable extrathoracic upper airway obstruction might be considered. The technical comments inform the reporter that the inspiratory loops are submaximal and, therefore, likely to be due to submaximal effort rather than pathology. Inspiratory loops are entirely effort dependent and maximal inspiratory effort is required to maximise the loops. Ensure flattened inspiratory loops are from maximal efforts before considering an associated pathology.

References

1 Borg BM, Hartley MF, Bailey MJ, Thompson BR. Adherence to acceptability and repeatability criteria for spirometry in complex lung function laboratories. Respir Care. 2012 Dec; 57(12):2032–8.
2 Ferguson GT, Enright PL, Buist AS, Higgins MW. Office spirometry for lung health assessment in adults: a consensus statement from the National Lung Health Education Program. Chest. 2000 Apr; 117(4):1146–61.
3 Miller MR, Hankinson J, Brusasco V, Burgos F, Casaburi R, Coates A, et al. Standardisation of spirometry. Eur Respir J. 2005 Aug; 26(2):319–38.

4 Wanger J, Clausen JL, Coates A, Pedersen OF, Brusasco V, Burgos F, et al. Standardisation of the measurement of lung volumes. Eur Respir J. 2005 Sep; 26(3):511–22.
5 Hughes JM, Pride NB. Examination of the Carbon Monoxide Diffusing Capacity (DLCO) in Relation to Its KCO and VA Components. Am J Respir Crit Care Med. 2012 Jul 15; 186(2):132–9.
6 Macintyre N, Crapo RO, Viegi G, Johnson DC, van der Grinten CP, Brusasco V, et al. Standardisation of the single-breath determination of carbon monoxide uptake in the lung. Eur Respir J. 2005 Oct; 26(4):720–35.
7 ATS/ERS Statement on respiratory muscle testing. Am J Respir Crit Care Med. 2002 Aug 15; 166(4):518–624.

CHAPTER 8

When the results do not fit the rules

As you become more proficient at interpretation and report writing, and increase the volume of reports you are writing, you will come across the occasional case that does not easily fit accepted interpretation strategies. This adds complexity to report writing and increases uncertainty. How do we account for:

- Borderline results? For example, a forced vital capacity (FVC) measured at 3.95 L with a lower limit of normal (LLN) of 4.00 L when all other parameters of spirometry are within normal limits.
- A response to inhaled bronchodilator (BD) that has a large absolute volume increase, but not a 12% increase? For example, an increase in FEV_1 by 10% and 0.45 L in response to inhaled bronchodilator in an individual with known asthma.
- Errors associated with extrapolating reference equations? For example, an extrapolated reference value may suggest a result is within normal limits, but in fact, the absolute value is low and may impact on function.

Lung function interpretation is not black and white, and there will be exceptions to the rules. Subjectivity, as discussed in Chapter 1, now comes into play. Often, it is the clinical background that brings context to allow a judgement to be made regarding normality or abnormality or change or no change. Sometimes, you may need to express your uncertainty in the significance of findings made. This last chapter focuses on cases that are not straightforward.

Case 1

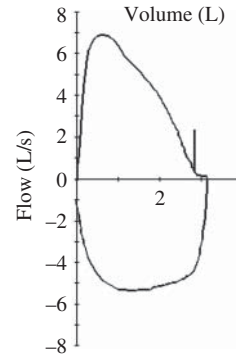
Ms Ava X is a 39-year-old female who first presented for respiratory review 14 months prior to the current visit with breathlessness. After multiple investigations

Interpreting Lung Function Tests: A Step-by-Step Guide, First Edition.
Brigitte M. Borg, Bruce R. Thompson and Robyn E. O'Hehir.
© 2014 John Wiley & Sons, Ltd. Published 2014 by John Wiley & Sons, Ltd.

she was diagnosed with pulmonary vasculitis. She also has iron-deficient anaemia, hypertension and obstructive sleep apnoea (OSA). She is currently taking oral corticosteroids (which have been problematic with weight gain), immunosuppressives, antihypertensives and iron supplements. She is due for a review. Lung function results are as follows:

Gender:	Female		
Age (yr):	39	Weight (kg):	176
Height (cm):	177	Race:	Caucasian
Clinical notes:	ILD, vasculitis. ?Progress		

	Normal range	Baseline	*z*-score
Spirometry			
FEV_1 (L)	>2.91	2.88	−1.71
FVC (L)	>3.61	3.20	−2.48
FEV_1/FVC (%)	>73	90	+1.26
Static lung volumes			
TLC (L)	5.03–6.79	4.81	−2.04
RV (L)	<2.47	1.70	−0.39
FRC (L)	2.45–4.17	1.92	−2.66
RV/TLC (%)	<40	35	+0.81
VC (L)	>3.61	3.10	
Single breath carbon monoxide transfer factor			
V_I (L)		3.07	
V_A (L)	>4.9	4.2	−2.68
T_LCO (mmol/min/kPa)	>6.6	13.5	+3.53
$T_LCO_{Hb\ corr}$ (mmol/min/kPa)		13.2	+3.33
KCO (mmol/min/kPa/L)	1.0–2.0	3.2	+6.36
$KCO_{Hb\ corr}$ (mmol/min/kPa/L)		3.1	+6.11
Hb (g/dL)		14.1	



Technical comment: Test performance was good. Patient commented that she has a previous history of pulmonary haemorrhage.

Previous results:

Date	This visit *13/02/2012*	*16/07/2011*	*14/11/2010*
FEV_1	2.88	3.24	3.02
FVC	3.20	3.75	3.58
FEV_1/FVC	90	86	84
TLC	4.81	4.89	
RV	1.70	1.39	
FRC	1.92	2.11	
RV/TLC	35	28	
V_A	4.2	4.7	4.5
T_LCO	13.5	8.6	8.7
$T_LCO_{Hb\ corr}$	13.2	8.9	10.5
KCO	3.2	1.8	1.9
$KCO_{Hb\ corr}$	3.1	1.9	2.3

Cautionary statements: The test is of good quality.

Technical interpretation: There appears to be a restrictive ventilatory defect on baseline spirometry; this is confirmed by a reduced TLC on static lung volumes. FRC is reduced in keeping with known obesity (BMI 56 kg/m^2). Alveolar volume is reduced and carbon monoxide transfer factor, corrected for haemoglobin, is within normal limits (markedly elevated).
Note: $KCO_{Hb\ corr}$ is elevated markedly. ?Current pulmonary haemorrhage. Possibly also a component of incomplete alveolar expansion.

Clinical context: In comparison to previous results on 16/7/2011, there has been a significant fall in FVC and a significant increase in $T_LCO_{Hb\ corr}$. The possibility of current pulmonary haemorrhage should be considered in the light of the markedly elevated T_LCO and KCO.

Final report: The test is of good quality. There is a restrictive ventilatory defect. FRC is reduced in keeping with known obesity (BMI 56 kg/m^2). Alveolar volume is reduced, and carbon monoxide transfer factor, corrected for haemoglobin, is within normal limits, but higher than expected. KCO is markedly elevated. In comparison with previous results from 16/7/2011, there has been a significant fall in FVC and a significant increase in T_LCO. In view of patient's history of pulmonary haemorrhage, current pulmonary haemorrhage should be considered (T_LCO and KCO *z*-scores > 1.96) as part of the clinical correlation.

Commentary: This case illustrates an example of when a finding in the normal range is actually abnormal. Most pathologies affecting gas exchange result in an abnormally low T_LCO, hence, generally only a LLN for T_LCO is set. In this case, the

T_LCO is markedly elevated (*z*-score > +3), KCO is above the upper limit of normal (ULN) (*z*-score > +6) and the alveolar volume is reduced (*z*-score < –2). These findings may represent incomplete alveolar expansion (e.g. chest wall restriction due to weight), microvascular dilation/congestion, increased pulmonary blood flow (e.g. post exercise, post pneumonectomy, obesity) or alveolar haemorrhage (1). Knowing the patient's history, current pulmonary haemorrhage should be considered. Even though the usefulness of the KCO is somewhat controversial (Chapter 4), this case is an example, although relatively rare, of when it can be useful.
When comparing current results to previous results, we note that the difference in FEV_1 measurements taken between 13/02/2012 and 16/07/2011 is 11% and 360 mL. This does not strictly satisfy the criteria for a significant change over time, but is a 360 mL fall in FEV_1 of clinical significance in this case? Possibly, and it may be worth mentioning. Alternatively, as the change in FVC during the same period is considered to be clinically significant, the borderline fall in FEV_1 may be of little consequence.

Case 2

Mrs Jenny Y, aged 74, presents for respiratory follow-up of her known asthma and bronchiectasis. Previous measurement of lung function has revealed a 'restrictive' pattern on spirometry.

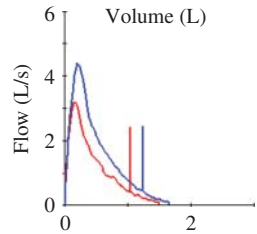
Gender:	Female	Date:	21/4/2012
Age (yr):	74	Weight (kg):	60
Height (cm):	150.2	Race:	Caucasian

Clinical notes: Asthma/bronchiectasis. Restriction on spirometry

	Normal range	Baseline	*z*-score	Post-BD	Change (%)
Spirometry					
FEV_1 (L)	>1.20	1.06	–2.10	1.27	+20
FVC (L)	>1.69	1.51	–2.14	1.67	+11
FEV_1/FVC (%)	>65	70	–0.82	76	
FEV_1/VC (%)	>65	66	–1.55	58	
Static lung volumes					
TLC (L)	3.45–5.20	4.10	–0.42	4.04	
RV (L)	<2.65	2.49	+1.22	1.86	
FRC (L)	1.60–3.31	2.83	+0.72	2.23	
RV/TLC (%)	<54	60	+2.72	46	
VC (L)	>1.69	1.61	–1.86	2.18	+16

	Normal range	Baseline	*z*-score	Post-BD	Change (%)
Single breath carbon monoxide transfer factor					
V_I (L)		1.52			
V_A (L)	>3.1	2.5	−2.68		
T_LCO (mmol/min/kPa)	>3.7	3.6	−1.65		
T_LCO $_{Hb\ corr}$ (mmol/min/kPa)		3.6	−1.73		
KCO (mmol/min/kPa/L)	0.8–1.6	1.5	+1.18		
$KCO_{Hb\ corr}$ (mmol/min/kPa/L)		1.4	+1.01		
Hb (g/dL)		14.1			

Technical comment: Test performance was good. Note: Age > 70 years – reference values for SLV and gas transfer have been extrapolated.



Previous results:

Date	*21/4/2012*[a]	*21/8/2011*	*17/11/2010*
FEV_1 – baseline	1.06	1.19	1.21
Post-BD	1.27	1.21	1.42
FVC – baseline	1.51	1.51	1.97
Post-BD	1.67	1.63	2.10
FEV_1/FVC – baseline	70	78	61
Post-BD	76	74	68
FEV_1/VC – baseline	66		
Post-BD	58		65
V_A	2.5		3.2
T_LCO	3.6		5.5
$T_L CO_{Hb\ corr}$	3.6		5.6
KCO	1.5		1.7
$KCO_{Hb\ corr}$	1.4		1.7

[a] Current visit.

(*continued*)

Cautionary statements:	The test is of good quality. Subject is >70 years and reference values for gas transfer and static lung volumes have been extrapolated and should be used with caution.
Technical interpretation:	There appears to be a restrictive ventilatory defect on baseline spirometry, however, baseline TLC is within normal limits and static lung volumes suggest gas trapping. There is a significant response to inhaled bronchodilator and post-BD FEV_1/VC<LLN, suggesting obstruction. Post-BD static lung volumes reveal resolution of gas trapping. Both alveolar volume and carbon monoxide transfer factor, corrected for haemoglobin, are reduced. As the KCO is in the normal range, the T_LCO may be reduced due to the reduction in alveolar volume, parenchymal or pulmonary vascular disease or a combination of these.
Clinical context:	In comparison to previous results on 21/8/2011, there has been no significant change in spirometry. However, in comparison to results from 17/11/2010, there has been a significant fall in FVC and $T_LCO_{Hb\ corr}$. Results on this occasion suggest an obstructive ventilatory defect with a reversible component. Gas exchange impairment is evident, but the cause is unclear.

Final report: Reference values for gas transfer and static lung volumes have been extrapolated for age and should be used with caution. The test is of good quality. Although there appears to be a restrictive ventilatory defect on baseline spirometry, TLC is within normal limits and static lung volumes show evidence of gas trapping. The response to inhaled bronchodilator is significant and reveals an obstructive ventilatory defect. Gas trapping appears to be resolved on post-bronchodilator static lung volumes. Both alveolar volume and carbon monoxide transfer factor, corrected for haemoglobin, appear to be reduced. Results suggest that the T_LCO may be reduced due to the reduction in alveolar volume, parenchymal or pulmonary vascular disease or a combination of these. In comparison to previous results on 21/8/2011, there has been no significant change in spirometry. However, in comparison to results from 17/11/2010, there has been a significant fall in FVC and $T_LCO_{Hb\ corr}$.
Results on this occasion suggest an obstructive ventilatory defect with a reversible component. Gas exchange impairment is evident, but the cause is unclear.
Commentary: This is a complex set of results with a number of competing issues. Firstly, the subject is 74 years old and the reference sets used in this book for gas transfer and static lung volumes are relevant for the age range 20–70 years. As we are extrapolating (or forecasting) how the reference values vary past this point, we need to add a cautionary statement to the report. Secondly, the baseline spirometry results suggest a restrictive ventilatory defect, while static lung volume measurements suggest an obstructive ventilatory defect. This highlights the limitations of using spirometry alone to diagnose restriction. Thirdly, the significant response in FEV_1 and the decrease in RV/TLC with inhaled bronchodilator give clarity that the predominant abnormality is indeed airflow obstruction. Although not routinely performed in many laboratories, repeating the static lung volume measurements post-BD is, in this case, very useful. All of this needs to be reported

in the context that the reference values being used for gas transfer and static lung volumes may not be correct.

Case 3

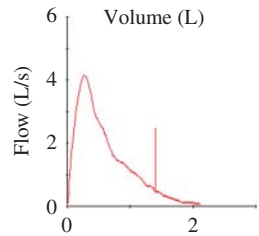
Ms Heidi R is a 71-year-old female with late-onset asthma. She has been noted to have a borderline low FVC on a previous spirometry test. She is referred for spirometry and static lung volume measurements.

Gender:	Female	Date:	12/2/2012
Age (yr):	71	Weight (kg):	69.5
Height (cm):	159	Race:	Caucasian

Clinical notes: Asthma. FVC borderline on last spirometry. ?TLC

	Normal range	Baseline	*z*-score	Post-BD	Change (%)
Spirometry					
FEV_1 (L)	>1.55	1.42	−2.02	1.50	+6
FVC (L)	>2.13	2.12	−1.67	2.18	+3
FEV_1/FVC (%)	>66	67	−1.47	69	
FEV_1/VC (%)	>66	53	−3.79		
Static lung volumes					
TLC (L)	3.96–5.72	5.90	+1.97		
RV (L)	<2.76	3.23	+2.87		
FRC (L)	1.90–3.62	3.51	+1.43		
RV/TLC (%)	<53	55	+2.04		
VC (L)	>2.13	2.67			

Technical comment: Test performance was good.



(*continued*)

Previous results:

Date	*12/2/2012*[a]	*16/3/2011*
FEV_1 – baseline	1.42	1.37
Post-BD	1.52	1.60
FVC – baseline	2.12	2.17
Post-BD	2.18	2.12
FEV_1/FVC – baseline	67	63
Post-BD	69	75
FEV_1/VC – baseline	53	-
Post-BD	-	-

[a] Current visit.

Cautionary statements: The test is of good quality. Reference values for static lung volumes have been extrapolated for age (>70 years) and should be used with caution.

Technical interpretation: There is an obstructive ventilatory defect (FEV_1/VC<LLN). Static lung volumes suggest possibly a large lung size with some evidence of gas trapping. The response to inhaled bronchodilator is not significant.

Clinical context: Results suggest obstruction with no response to inhaled bronchodilator on this occasion. In comparison to previous results on 13/3/2011, there has been no significant change in spirometry.

Final report: Reference values for static lung volumes have been extrapolated for age and should be used with caution. The test is of good quality. There is an obstructive ventilatory defect with evidence of gas trapping. Static lung volumes also suggest large lung size. The response to inhaled bronchodilator is not significant. In comparison to previous results on 13/3/2011, there has been no significant change in spirometry.

Commentary: On examination of the forced spirometry results alone, there appears to be a borderline spirometry result – FVC and FEV_1/FVC at LLN. This makes interpretation difficult. The addition of static lung volumes reveals that FVC is likely to be reduced due to airflow limitation (TLC > LLN and RV/TLC > ULN) and confirms obstruction as FEV_1/VC (from static lung volumes) is reduced. TLC is elevated, but FRC is not – this suggests large lung size also.

In addition to these findings, the age of the subject and its impact on the reference values need to be considered. The reference sets used in this book for static lung volumes are relevant for the age range 20–70 years.

Case 4

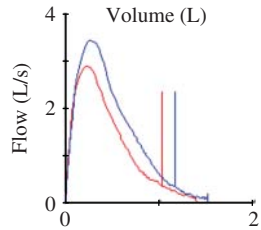
Miss Martha L is a 76-year-old lady referred from her local doctor for breathing tests. She has a 40 pack year smoking history and is thought to have COPD based on symptoms, but has not had formal lung function tests previously. It has been noted that she has become more short of breath over recent months.

Gender:	Female		
Age (yr):	76	Weight (kg):	65
Height (cm):	139.4	Race:	Caucasian

Clinical notes: COPD, dyspnoea on exertion

	Normal range	Baseline	*z*-score	Post-BD	Change (%)
Spirometry					
FEV_1 (L)	>0.84	1.04	−0.89	1.18	+13
FVC (L)	>1.23	1.39	−1.12	1.54	+11
FEV_1/FVC (%)	>65	75	+0.03	77	

Technical comment: Test performance was good.



Previous results: Nil

Cautionary statements: The test is of good quality. Reference values for spirometry have been extrapolated for height and should be used with caution.

Technical interpretation: Baseline ventilatory function appears to be within normal limits. The response to inhaled bronchodilator is not significant.

Clinical context: The results appear to be inconsistent with the spirometric definition of COPD. Note: Although the results appear to be within the normal range (being mindful that the normal range has been extrapolated), the absolute values are small and this may impact on function.

Final report: The reference values have been extrapolated for height (139 cm) and should be used with caution. The test is of good quality. Baseline ventilatory function appears to be within normal limits. The response to inhaled bronchodilator is not significant. Results appear to be inconsistent with the spirometric definition of COPD. In addition, although the results appear to be within normal limits, the absolute values are small and this may impact on function.

Commentary: The reference values in this case have been extrapolated for height as the subject is only 139 cm, but the lower limit of the height range for the reference set used in this book is 144 cm. Therefore, the results should be

interpreted with caution. The LLN for FEV_1 (0.84 L) and FVC (1.23 L) are quite low, and although the results appear to be within the normal range, the absolute values are small and this may impact on the subject's functional status. It is important to note these facts.

Case 5

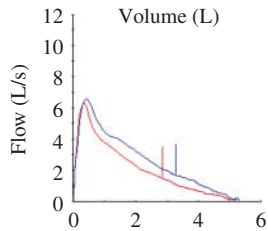
Mr Kevin D is a 20-year-old male with known asthma. He continues to complain of symptoms despite being on combination therapy and using a reliever regularly. He is referred for spirometry to assess his asthma control.

Gender:	Male	Date:	04/04/2012
Age (yr):	20	Weight (kg):	62.1
Height (cm):	169.5	Race:	Caucasian

Clinical notes: Asthma

	Normal range	Baseline	*z*-score	Post-BD	Change (%)
Spirometry					
FEV_1 (L)	>3.56	2.85	−3.27	3.30	+16
FVC (L)	>4.22	5.16	+0.18	5.28	+2
FEV_1/FVC (%)	>74	55	−4.88	63	

Technical comment: Test performance was good. Salbutamol and eformeterol/budesonide taken 2 h prior to test.



Previous results:

Date	*04/04/2012*[a]	*12/01/2012*	*17/6/2011*	*14/5/2011*
FEV_1 – baseline	2.85	2.90	2.97	2.47
Post-BD	3.30	3.28	2.88	2.88
FVC – baseline	5.16	4.54	4.25	4.33
Post-BD	5.28	4.51	4.19	4.22
FEV_1/FVC – baseline	55	64	70	57
Post-BD	63	73	69	68

[a] Current visit.

Cautionary statements:	The test is of good quality.
Technical interpretation:	There is an obstructive ventilatory defect. The response to inhaled bronchodilator is significant with incomplete reversibility of airflow limitation.
Clinical context:	Note the significant bronchodilator response despite use of a short- and long-acting bronchodilator 2 h prior to test. Results suggest suboptimal asthma control though clinical correlation is required. In comparison to previous results from 12/1/2012, there has been a significant increase in FVC.

Final report: The test is of good quality. There is an obstructive ventilatory defect. The response to inhaled bronchodilator is significant with incomplete reversibility of airflow limitation. Note that a significant bronchodilator response is seen despite use of short- and long-acting bronchodilators 2 hours prior to testing. In comparison to previous results from 12/1/2012, there has been a significant increase in FVC. Results suggest suboptimal asthma control though clinical correlation is required.
Commentary: This case illustrates the usefulness of knowing the prescribed medications. Despite being on a combination medication (symptom controller and preventer) and a reliever, this man has a significant response to inhaled bronchodilator 2 h after bronchodilators have been taken. This finding may be due to poor adherence to therapy, poor inhaler technique, poor asthma control with the current prescribed medication doses or a combination of these factors.

Case 6

Mrs Milla K is a 41-year-old female. She has recently been diagnosed with limited scleroderma with Raynaud's phenomena. She has also scoliosis, with Harrington's rods inserted at 10 years of age. A recent chest X-ray shows moderate scoliosis with rods *in situ*; lung fields are clear. Her rheumatologist has referred her for lung function tests to see if there is evidence of interstitial lung disease or pulmonary hypertension.

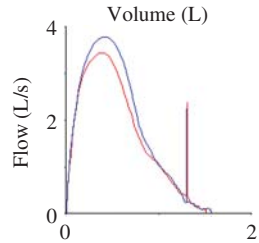
Gender:	Female		
Age (yr):	41	Weight (kg):	67
Height (cm):	168	Race:	Caucasian
Clinical notes:	Scleroderma. ?evidence of ILD or pulmonary hypertension. Scoliosis – rod inserted at age 10.		

	Normal range	Baseline	*z*-score	Post-BD	Change (%)
Spirometry					
FEV_1 (L)	>2.58	1.32	−4.96	1.32	0
FVC (L)	>3.21	1.51	−5.43	1.57	+ 4
FEV_1/FVC (%)	>72	87	+0.89	84	
FEV_1/VC (%)	>72	86	+0.70		

(*continued*)

	Normal range	Baseline	*z*-score	Post-BD	Change (%)
Static lung volumes					
TLC (L)	4.50–6.25	2.77	−4.86		
RV (L)	<2.34	1.25	−1.21		
FRC (L)	2.14–3.85	1.43	−2.99		
RV/TLC (%)	<40	45	+2.49		
VC (L)	>3.21	1.52			
Single breath carbon monoxide transfer factor					
V_I (L)			1.53		
V_A (L)	>4.3	2.4	−4.50		
T_LCO (mmol/min/kPa)	>6.1	3.7	−3.42		
$T_LCO_{Hb\ corr}$ (mmol/min/kPa)		3.8	−3.34		
KCO (mmol/min/kPa/L)	1.0–2.1	1.5	−0.05		
$KCO_{Hb\ corr}$ (mmol/min/kPa/L)		1.6	+0.20		
Hb (g/dL)		12.5			

Technical comment: Test performance was good.



Cautionary statements: The test is of good quality.

Technical interpretation: There appears to be a restrictive defect on spirometry. This is confirmed with a reduced TLC on static lung volumes. Note that RV/TLC is elevated. There is no evidence of obstruction on spirometry, so unlikely to be due to gas trapping/airflow limitation. The elevated RV/TLC may be due to chest wall/respiratory muscle dysfunction from scoliosis. The response to inhaled bronchodilator is not significant.
Both alveolar volume and carbon monoxide transfer factor, corrected for haemoglobin, are reduced. As the KCO is in the normal range, the T_LCO may be reduced due to the reduction in alveolar volume, parenchymal or pulmonary vascular disease or a combination of these.

Clinical context: There is a restrictive ventilatory defect that may reflect interstitial lung disease or known scoliosis. The elevated RV/TLC may reflect respiratory muscle/chest wall dysfunction due to known scoliosis. Gas exchange is impaired. ILD or pulmonary hypertension cannot be ruled out.

Final report: The test is of good quality. There is a restrictive ventilatory defect. The RV/TLC is elevated, possibly reflecting chest wall/respiratory muscle dysfunction in keeping with known scoliosis. The response to inhaled bronchodilator is not significant. Both the alveolar volume and carbon monoxide transfer factor, corrected for haemoglobin, are reduced. Results suggest that the T_LCO may be reduced due to the reduction in alveolar volume, parenchymal or pulmonary vascular disease or a combination of these. In conclusion, there is a restrictive defect that may reflect interstitial lung disease or known scoliosis. There may be some chest wall/respiratory muscle dysfunction related to known scoliosis. Gas exchange is impaired, but the cause is not clear. ILD and/or pulmonary hypertension cannot be excluded. Clinical correlation is required.
Commentary: In this example, the restrictive ventilatory defect resulting from the moderate scoliosis dominates other pathophysiological abnormalities. The cause of the gas exchange abnormality is difficult to identify because the KCO is within the normal range. Hence, the report ends up being quite inconclusive for the referring physician. This is not a limitation of the report per se, but more that in this case, the tests ordered are not able to discriminate a pure gas exchange abnormality in the presence of a restricted lung.

Case 7

Ms Carol S is a 61-year-old female with a past history of asthma. She has recently been diagnosed with atrial fibrillation and commenced on a non-selective beta-blocker. She has been admitted for investigation after presenting to the emergency department complaining of increasing dyspnoea occurring with minimal exertion over the past few weeks, culminating in an acute episode resulting in syncope. The cardiology unit is wondering if there is any reversible airways disease.

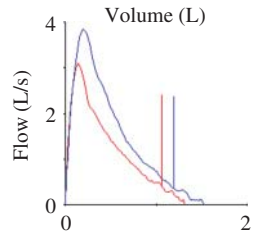
Gender:	Female		
Age (yr):	61	Weight (kg):	98
Height (cm):	160.5	Race:	Caucasian
Clinical notes:	Increasing dyspnoea on minimal exertion over weeks. Past history mild asthma. Atrial fibrillation – recently started on sotalol. ?reversible obstructive airways disease.		

	Normal range	Baseline	*z*-score	Post-BD	Change (%)
Spirometry					
FEV_1 (L)	>1.88	1.07	−3.99	1.20	+12
FVC (L)	>2.51	1.33	−4.51	1.52	+14
FEV_1/FVC (%)	>68	80	+0.44	79	
FEV_1/VC (%)	>68	71	−1.17		

(*continued*)

	Normal range	Baseline	*z*-score	Post-BD	Change (%)
Static lung volumes					
TLC (L)	4.05–5.81	3.32	−3.01		
RV (L)	<2.59	1.81	−0.41		
FRC (L)	1.93–3.64	2.04	−1.42		
RV/TLC (%)	<49	55	+2.80		
VC (L)	>2.51	1.51	−4.07		
Single breath carbon monoxide transfer factor					
V_I (L)		1.44			
V_A (L)	>3.8	2.7	−3.55		
$T_L CO$ (mmol/min/kPa)	>5.3	3.8	−3.25		
$T_L CO_{Hb\ corr}$ (mmol/min/kPa)		4.2	−2.89		
KCO (mmol/min/kPa/L)	1.0–1.8	1.4	−0.03		
$KCO_{Hb\ corr}$ (mmol/min/kPa/L)		1.5	+0.63		
Hb (g/dL)			11.1		

Technical comment: Test performance was good.



Previous results: Nil

Cautionary statements: The test is of good quality.

Technical interpretation: Note: BMI is 38 kg/m^2

There appears to be a restrictive defect on spirometry. This is confirmed with a reduced TLC on static lung volumes. Note that RV/TLC is elevated and the response to inhaled bronchodilator is borderline significant (not quite 200 mL increase in FVC), suggesting obstruction. A mixed/obstructive defect should be considered.

Both alveolar volume and carbon monoxide transfer factor, corrected for haemoglobin, are reduced. As the KCO is in the normal range, the $T_L CO$ may be reduced due to the reduction in alveolar volume, parenchymal or pulmonary vascular disease or a combination of these.

Clinical context: A mixed obstructive/restrictive ventilatory defect should be considered. Reversible airflow limitation should be considered. Gas exchange impairment is evident, though the cause is not clear. No previous results are available for comparison.

Final report: The test is of good quality. There is a restrictive ventilatory defect. RV/TLC is elevated and there is a borderline significant response to inhaled bronchodilator, suggesting airflow obstruction also. A mixed obstructive/restrictive ventilatory defect should be considered. Both alveolar volume and carbon monoxide transfer factor, corrected for haemoglobin, are reduced. The T_LCO may be reduced due to the reduction in alveolar volume, parenchymal or pulmonary vascular disease or a combination of these. No previous results are available for comparison. Summary: A mixed obstructive/restrictive defect should be considered. Reversible airflow limitation should be considered. Gas exchange impairment is evident, though the cause is not clear. Clinical correlation is required.
Commentary: This is another complicated case with a number of aspects for consideration. Baseline ventilatory function shows a restrictive pattern. The elevated RV/TLC and the borderline significant response to inhaled bronchodilator in FVC suggest that airflow obstruction should be considered as well.
The response to inhaled bronchodilator does not strictly meet the criteria for a significant response. Although one could say there was no significant response to inhaled bronchodilator, the referring physician was specifically looking for reversible obstructive airways disease and the response is borderline (+14% and 190 mL), so it is probably worth mentioning. Because the response is not clear cut, the phrase 'borderline significant' which is 'suggestive' of airflow obstruction is used. This feeds back to the referring physician that it is not clear cut, but may suggest obstruction. Using these results with the clinical picture may make the overall picture clearer.

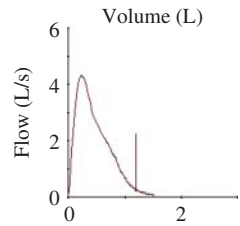
Case 8

Ms Harriet D is a 39-year-old female who has recently undergone a bilateral sequential lung transplant (BSLTx) for bronchiectasis. Four days after discharge from the intensive care unit post-procedure, Harriet was found in respiratory distress and noted to be hypercapnic. Bi-level ventilation was started with good effect. A sleep study showed prolonged periods of desaturation with a rising transcutaneous CO_2 and hypopnoeas, consistent with hypoventilation. Diaphragm screening showed diminished excursion of the left hemidiaphragm during inspiration, expiration and sniff test. No paradoxical motion was noted. She is discharged home with non-invasive ventilation. Her lung function is measured prior to review:

Gender:	Female	Date:	22/3/2012
Age (yr):	39	Weight (kg):	70.9
Height (cm):	170	Race:	Caucasian
Clinical notes:	8 weeks post-BSLTx for bronchiectasis. ?diaphragm weakness, ?myopathy		

(*continued*)

	Normal range	Baseline Upright	*z*-score	Baseline Supine	Change (%)
Spirometry					
FEV_1 (L)	>2.68	1.25	−5.32		
FVC (L)	>3.32	1.51	−5.58		
VC (L)	>3.32	1.54	−5.51	1.04	−32
FEV_1/FVC (%)	>73	83	+0.04		
FEV_1/VC (%)	>73	81	−0.23		
Single breath carbon monoxide transfer factor					
V_I (L)		1.53			
V_A (L)	>4.4	2.4	−4.69		
T_LCO (mmol/min/kPa)	>6.2	2.9	−4.13		
$T_LCO_{Hb\ corr}$ (mmol/min/kPa)		3.2	−3.93		
KCO (mmol/min/kPa/L)	1.0–2.1	1.2	−1.17		
$KCO_{Hb\ corr}$ (mmol/min/kPa/L)		1.3	−0.80		
Hb (g/dL)		11.1			
Maximal respiratory pressures					
$P_I$max (cmH_2O)	>50	86	−0.03		
$P_E$max (cmH_2O)	>72	105	0.14		
sNIP (cmH_2O)	>58	70	−0.95		
Technical comment:		Test performance was good.			



Previous results:

Date	*22/3/2012*[a]	*4/3/2012*
FEV_1 – baseline	1.25	0.90
FVC – baseline	1.51	1.12
FEV_1/FVC – baseline	83	80
VC upright	1.54	
VC supine	1.04	
$P_I$max	86	
$P_E$max	105	
sNIP	90	

[a] Current visit.

Cautionary statements:	The test quality is good.
Technical interpretation:	There appears to be a restrictive ventilatory defect. Static lung volumes are suggested to confirm restriction. Both the alveolar volume and carbon monoxide transfer factor, corrected for haemoglobin, are reduced. As the KCO is in the normal range, the T_LCO may be reduced due to the reduction in alveolar volume, parenchymal or pulmonary vascular disease or a combination of these. Maximal respiratory pressures and sNIP are within normal limits, suggesting that global respiratory muscle weakness is unlikely. The fall in vital capacity from upright to supine posture suggests significant diaphragm weakness (>30%), however, in the presence of a preserved $P_I$max and sNIP, this is unlikely.
Clinical context:	In comparison to previous results on 4/3/2012, there has been a significant increase in FEV_1 and FVC. Gas exchange is impaired, though the cause is not clear. Overall respiratory muscle function appears to be intact, though some diaphragm weakness cannot be excluded.

Final report: The test is of good quality. There appears to be a restrictive ventilatory defect and measurements of static lung volumes are suggested to confirm restriction. Both the alveolar volume and carbon monoxide transfer factor, corrected for haemoglobin, are reduced. The T_LCO may be reduced due to the reduction in alveolar volume, parenchymal or pulmonary vascular disease or a combination of these. The fall in vital capacity from upright to supine posture suggests significant diaphragm weakness, however, in the presence of a preserved $P_I$max and sNIP, this is unlikely. $P_E$max is within the normal range. In comparison to previous results from 4/3/2012, there has been a significant improvement in FEV_1 and FVC. Summary: Ventilatory function is impaired (possible restriction). Gas exchange is impaired though the cause is uncertain. Global respiratory muscle function appears to be intact, though some diaphragm weakness cannot be excluded.

Commentary: As discussed in Chapter 5, using multiple methods for assessing respiratory muscle strength may reduce the false-positive rate for respiratory muscle weakness. In this case, both $P_I$max and sNIP are in the normal range, while the difference in VC between upright and supine postures is elevated (>30%). The likelihood of significant diaphragm weakness is reduced because of the preserved $P_I$max and sNIP. Also, from the diaphragm screening, the lack of paradoxical movement suggests that diaphragm has sufficient strength to prevent the abdominal contents from pushing up into the thorax. So while some diaphragm weakness cannot be excluded, it is probably not substantial.

The other difficult aspect of this case is consideration of the lung transplant procedure and the donor lungs. What is the impact of the transplant procedure and the donor lungs themselves on overall chest wall and lung mechanics? Are the reference values of relevance anymore?

Case 9

Miss Angela B is 30-year-old female who has presented to her local doctor to complete a fitness to dive assessment. She has a past history of bi-basal pneumonia, and spirometry performed by her local doctor shows obstruction with no significant response to inhaled bronchodilator. He refers her for further evaluation.

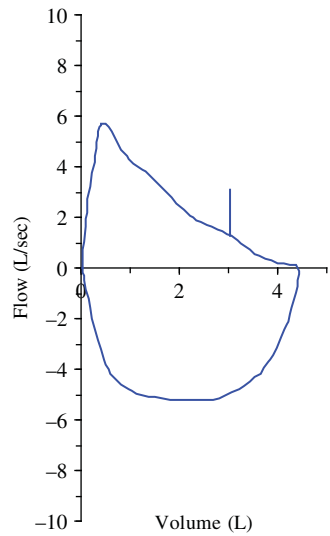
Gender:	Female		
Age (yr):	30	Weight (kg):	65.5
Height (cm):	170	Race:	Caucasian

Clinical notes: ?asthma ?Fit to dive. Past history bi-basal pneumonia. Low FEV_1/FVC.

	Normal range	Baseline	*z*-score
Spirometry			
FEV_1 (L)	>2.81	3.00	−1.15
FVC (L)	>3.35	4.45	+0.76
FEV_1/FVC (%)	>75	67	−2.86

Challenge:	Mannitol									
Dose (mg)	0	5	15	35	75	155	315	475	635	Post-BD
FEV_1 (L)	2.97	2.85	2.85	2.88	2.79	2.85	2.79	2.73	2.64	3.33
Change (%)	0	−4	−4	−3	−7	−4	−7	−9	−12	+12
PD15 (mg)	>635									

Technical comment: Test performance was good. Note: obstruction on baseline spirometry.
Test preparation requirements met.



Previous results: No previous results from this centre.

Cautionary statements:	The test quality is good.
Technical interpretation:	Baseline ventilatory function reveals an obstructive ventilatory defect. The response to inhaled mannitol is negative. Of note, however, is a significant response to inhaled bronchodilator between first mannitol dose (0 mg) and post-BD FEV_1.
Clinical context:	No previous results are available for comparison. Asthma should be considered.

Final report: The test performance was good. Baseline ventilatory function reveals an obstructive ventilatory defect. The response to inhaled mannitol is negative; however, there is a significant response to inhaled bronchodilator (compared to FEV_1 from the 0 mg mannitol dose). Asthma should be considered as part of the clinical correlation.

Commentary: In this case, the patient has obstruction on baseline spirometry. She has previously been shown to have non-reversible airway obstruction according to the referral, so a challenge test has been performed.

Although the mannitol challenge is negative (<15% fall in FEV_1 after 635 mg inhaled mannitol), the response to inhaled bronchodilator from baseline spirometry is 11% and 330 mL and from the baseline mannitol dose (0 mg) is 12% and 360 mL. This suggests that there is some reversibility and asthma should be considered.

A negative mannitol challenge does not exclude asthma because the sensitivity of the test is low. The response to inhaled bronchodilator suggests that asthma is a possible diagnosis.

Case 10

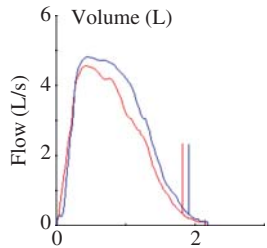
Mrs Helen M[c] is a 70-year-old female. She is obese with a BMI of 41 kg/m^2 and has known OSA, diagnosed 10 years prior. She is on nocturnal ventilation with continuous positive airway pressure of 15 cm H_2O and is seen in the sleep clinic for annual review. On her recent visit, she has commented that she feels occasional wheeze. Her sleep physician has referred her for spirometry.

Gender:	Female	Date:	1/4/2013
Age (yr):	70	Weight (kg):	102
Height (cm):	158	Race:	Caucasian

Clinical notes: OSA, wheeze

	Normal range	Baseline	*z*-score	Post-BD	Change (%)
Spirometry					
FEV_1 (L)	>1.55	1.83	−0.80	1.92	+5
FVC (L)	>2.13	2.14	−1.61	2.18	+2
FEV_1/FVC (%)	>66	86	+1.61	88	

Technical comment: Test performance was good.



Previous results:

Date	*1/4/2013*[a]	*10/5/2003*
Weight	102	98
FEV_1 – baseline	1.83	2.14
Post-BD	1.92	2.27
FVC – baseline	2.14	2.59
Post-BD	2.18	2.66
FEV_1/FVC – baseline	86	83
Post-BD	88	85

[a] Current visit.

Cautionary statements:	The test is of good quality.
Technical interpretation:	Note: BMI is 41 kg/m^2 Baseline ventilatory function is within normal limits (note: FVC is at the LLN). The response to inhaled bronchodilator is not significant.
Clinical context:	In comparison to results from 10/5/2003, there appears to have been a significant fall in FEV_1 and FVC, though this may be, in part, due to normal lung ageing. No apparent airflow limitation on this occasion.

Final report: The test is of good quality. Note: BMI 41 kg/m^2. Baseline spirometry is within normal limits, with no response to inhaled bronchodilator. In comparison to results from 10/5/2003, there appears to have been a significant fall in FEV_1 and FVC, though this, in part, may be due to normal lung ageing.
Commentary: This woman's baseline spirometry is within normal limits, though FVC is at the LLN. This may be due to her morbid obesity or could be normal for her – static lung volumes may provide some more information.
In this case, previous spirometry used to track changes over time is from 10 years prior. We know that FEV_1 and FVC decline as age increases once we have reached peak lung function somewhere between 20 and 25 years of age. Studies suggest that in healthy individuals, a loss in volume of up to 30 mL in FEV_1 and FVC per year is possible (2–4). The falls in FEV_1 and FVC over 10 years are 350 and 480 mL, respectively. Hence, we cannot exclude that part of her decline in lung function over the period may be due to normal lung ageing.

References

1 Hughes JM, Pride NB. Examination of the carbon monoxide diffusing capacity (DLCO) in relation to its KCO and VA components. Am J Respir Crit Care Med. 2012 Jul 15; 186(2):132–9.
2 Xu X, Laird N, Dockery DW, Schouten JP, Rijcken B, Weiss ST. Age, period, and cohort effects on pulmonary function in a 24-year longitudinal study. Am J Epidemiol. 1995 Mar 15; 141(6):554–66.
3 Speizer FE, Tager IB. Epidemiology of chronic mucus hypersecretion and obstructive airways disease. Epidemiol Rev. 1979; 1:124–42.
4 Fletcher C, Peto R. The natural history of chronic airflow obstruction. Br Med J. 1977 Jun 25; 1(6077):1645–8.

Glossary

% Pred	Percentage of the mean predicted value
(F)VC	Forced vital capacity or vital capacity – whichever is larger
AHR	Airway hyper-responsiveness
BD	Bronchodilator
BMI	Body mass index. Units: kg/m^2
cm	Centimetres
cmH_2O	Centimetres of water – unit of pressure
CO	Carbon monoxide
COHb	% haemoglobin with carbon monoxide bound to it
COPD	Chronic obstructive pulmonary disease
CR	Coefficient of repeatability: two times the standard deviation of the differences between measures
dL	Decilitre
D_LCO	Carbon monoxide diffusing capacity. Also known as transfer factor (T_LCO)
EVH	Eucapnic voluntary hyperventilation or hyperpnoea
$FEF_{25-75\%}$	The mean forced expiratory flow between 25% and 75% of the FVC; normally reported in L/s. Also called $MEF_{25-75\%}$ or MMEF (maximum mid-expiratory flow)
FEF_{50}	Forced expiratory flow at 50% of the FVC. Units: L/s
FEV_1	Forced expiratory volume in 1 s

Interpreting Lung Function Tests: A Step-by-Step Guide, First Edition.
Brigitte M. Borg, Bruce R. Thompson and Robyn E. O'Hehir.
© 2014 John Wiley & Sons, Ltd. Published 2014 by John Wiley & Sons, Ltd.

$FEV_{1/}$(F)VC	The ratio of FEV_1 to FVC or VC
FIF_{50}	Forced inspiratory flow at 50% of the FIVC. Units: L/s
FIVC	Forced inspiratory vital capacity
FRC	Functional residual capacity
FVC	Forced vital capacity
g	Grams
Hb	Haemoglobin
Hbcorr	Value corrected for haemoglobin level
HRCT	High-resolution computed tomography
h	Hours
ICS	Inhaled corticosteroids
ILD	Interstitial lung disease
KCO	Transfer coefficient of carbon monoxide.
kg	Kilograms
kPa	Kilopascal – unit of pressure
L	Litres
LLN	Lower limit of the normal range
m	Metre
MEP	Maximal expiratory pressure
mg	Milligrams
min	Minutes
MIP	Maximal inspiratory pressure
mL	Millilitres
mmol	Millimole – unit of concentration
MPV	Mean predicted value
Mueller manoeuvre	The action of making a forced inspiratory effort with a closed airway (often closed epiglottis)
MVV	Maximum voluntary ventilation
O_2	Oxygen
OSA	Obstructive sleep apnoea
P_AO_2	Partial pressure of oxygen in the alveoli
PC*x*	Provoking concentration at which a *x*% fall in FEV1 is achieved
PD*x*	Provoking dose at which a *x*% fall in FEV1 is achieved
PEF	Peak expiratory flow
$P_E$max	Maximal expiratory pressure
$P_I$max	Maximal inspiratory pressure
P_IO_2	Partial pressure of inspired oxygen
pO_2	Partial pressure of oxygen

post-BD	Post bronchodilator
RSD	Residual standard deviation
RV	Residual volume
RV/TLC	The ratio of residual volume to total lung capacity
s	Seconds
SI units	International System of Units
SLV	Static lung volumes
sNIP	Sniff nasal inspiratory pressure
SVC	Slow vital capacity
TLC	Total lung capacity
T_LCO	Carbon monoxide transfer factor. Also known as diffusing capacity (D_LCO)
ULN	Upper limit of the normal range
V_A	Alveolar volume
Valsalva manoeuvre	The action of making a forced expiratory effort with a closed airway (often closed epiglottis)
VC	Vital capacity
V_I	Inspired volume
yr	Years
z-score	The number of standard deviations the measured value is from the mean predicted value

Index

Figures and tables are indicated by '*f*' and '*t*' respectively

airway hyper-responsiveness (AHR)
  bronchial provocation tests, 99, 101
  ICS, 102
amyloid myopathy, 87–88
asthma
  bronchial provocation test, 23, 108, 109, 112
  corticosteroid, 7–8
  exercise-induced, 106, 107, 113, 114, 115
  obstructive ventilatory defect, 5
  poor quality test, 122–123, 134, 135
  spirometry, 26, 32, 33
  static lung volume, 44–45
  T_LCO, 68–69, 71
atopic asthma, 110
atrial fibrillation, 151–153

BD. *See* bronchodilator (BD)
bi-basal pneumonia, 156–157
breathlessness, 96–97, 139
bronchial provocation tests
  airway responsiveness, 100
  asthma, 101, 104*t*, 107–110
  chronic cough, 106–107
  clinical context, indirect challenges, 102, 104*t*
  comparisons, 103
  direct challenges, 99
  evaluation, 101–103*t*
  exercise-associated asthma, 113, 114, 115
  inhalation challenges, 100
  interpretation, 101–104
  medications and foods to avoid, 100*t*
  methacholine challenges, 101
  nocturnal cough, wheeze on exertion, 111
  paroxysmal shortness of breath, 105–106
  physical challenges, 100
  provoking dose (PD), 100
  sensitivity/specificity data, 101–102, 104*t*
  severity scales, 102
  test quality, 101
  types, 99
  wheeze on exertion, 112
bronchiectasis, 5, 25, 72, 142–145, 153–155
bronchoconstriction, 99, 101, 114, 135
bronchodilator (BD)
  AHR, 101
  asthma, 23
  baseline spirometry, 18

Interpreting Lung Function Tests: A Step-by-Step Guide, First Edition.
Brigitte M. Borg, Bruce R. Thompson and Robyn E. O'Hehir.

© 2014 John Wiley & Sons, Ltd. Published 2014 by John Wiley & Sons, Ltd.

bronchodilator (BD) (*continued*)
reversibility, 99
spirometry before and after, 18

carbon monoxide diffusing capacity (D_LCO), 53
carbon monoxide transfer factor (T_LCO)
alveolar pO_2, 57
alveolar volume, 57
amiodarone, 73–74
application, 60–61
asthma, 71–72
bronchial provocation test, 68–69
carboxyhaemoglobin (COHb), 56
comparison to previous results, 60
congestive cardiac failure, 66–67
COPD, emphysema, 63–64
D_LCO, 53
factors affecting, 55, 56*t*
haemoglobin (Hb), 55–56
Hodgkin's lymphoma, 77–78
interstitial lung disease, 70–71, 75–76
limits, normal range, 58–59, 59*t*
obesity hypoventilation syndrome, 64–65
parameters, 53, 54, 58
pulmonary capillary blood volume, 57
single breath carbon monoxide transfer factor, 53, 54*f*
test quality, 54–55
TLC, 53
transfer coefficient, KCO, 57, 59–60
chronic cough, 106–107, 124–129
chronic obstructive pulmonary disease (COPD), 24–25, 28, 42, 50, 94–95
coefficient of repeatability (CR), 5–8
COPD. *See* chronic obstructive pulmonary disease (COPD)
cough and dyspnoea, 92–93
CR. *See* coefficient of repeatability (CR)

diaphragm paralysis, 84–85
dyspnoea on exertion, 146–148, 151–153

eucapnic voluntary hyperpnea (EVH), 99, 103, 104, 113, 114, 115
exercise-associated asthma, 113, 114, 115

forced vital capacity (FVC)
and COPD, 28
spirometry, 13–14
functional residual capacity (FRC), 38, 79, 80, 86
FVC. *See* forced vital capacity (FVC)
FVC borderline, 145–146

Global Lung Initiative, 2

Hx of childhood asthma, 107
hyper-reactive airways, 21

inspiratory/expiratory muscle dysfunction, 81, 82
inspiratory muscle weakness, 82, 132
inspiratory vital capacity (IVC), 119
interpretation
clinical question in referral, 8
comparison, 5–8
CR, 5–8
detected abnormality classification, 4–5
normality/abnormality, 3–4
pattern of abnormality, 4–5
reference values, assessment, 2–3
severity of abnormality, 5, 6*t*
test validity, 1–2
IVC. *See* inspiratory vital capacity (IVC)

LLN. *See* lower limits of normal (LLN)
lower limits of normal (LLN), 3–4

maximal expiratory pressure ($P_E$max/MEP), 79, 80
maximal inspiratory pressure ($P_I$max/MIP), 79, 80
mean predicted value (MPV), 3
mild asthma, 151–153
mitral valve repair, 92–93
motor neuron disease, probable, 131–133

MPV. *See* mean predicted value (MPV)
myopathy, 153–155
myotonic dystrophy, 86

nocturnal cough, 111
normality/abnormality, determining. *See also* interpretation
  LLN, 3–4
  MPV, 3
  normal range, definition, 3–4
  RSD, 3
  ULN, 3

paroxysmal shortness of breath, 105–106
PD. *See* provoking dose (PD)
$P_E$max/MEP. *See* maximal expiratory pressure ($P_E$max/MEP)
phrenic nerve damage, 92–93
$P_I$max/MIP. *See* maximal inspiratory pressure ($P_I$max/MIP)
pneumonia, 129–130, 136–137
polymyositis, 88–89
post-BSLTx, 153–155
provoking dose (PD), 100
pulmonary hypertension, 149–151

quality tests
  assessment, 117, 119, 120
  factors, 117, 118*t*
  rating scales, 117, 118*t*
  spirometry, 118*t*
  suboptimal, 119–120
    asthma, 122–123, 134–137
    chronic cough, 124–125
    lung mass, baseline spirometry, 121
    pneumonia, 129–130, 136–137
    probable motor neuron disease, 131–133

report writing, features
  subjectivity, 10–11
  technical interpretation *vs.* clinical context, 9–10
residual standard deviation (RSD), 3
respiratory muscle impairment, 131–133
respiratory muscle strength
  amyloid myopathy, 87–88
  breathlessness, 96–97
  comparisons, 82
  cough and dyspnoea, 92–93
  measurement, 79, 83*t*
  myotonic dystrophy, 86
  normal range limits, 81–82
  parameters, interpretation, 81
  polymyositis, 88–89
  right diaphragm paralysis, 84–85
  SLE, 90–92
  steps, interpretation, 84
  test quality, 80
reversible obstructive airways disease, 151–153
RSD. *See* residual standard deviation (RSD)

scleroderma, 149–151
scoliosis, 149–151
severe systemic lupus erythematosus (SLE), 90–92
slow vital capacity (SVC), 119
SLV. *See* static lung volume (SLV)
sniff nasal inspiratory pressure (sNIP), 79–82, 87, 88, 95
spirometry
  asthma, 23–24, 26–27, 32–34
  baseline, 9, 18, 23, 34, 44, 45, 46, 48, 50, 62, 67, 69, 76, 100, 106, 121, 128, 135, 144, 157, 159
  BD. *see* bronchodilator (BD)
  bronchiectasis, 25–26
  cancer, trachea, 30
  comparisons, 19
  COPD, 24–25, 28
  FVC borderline, 145–146
  hyper-reactive airways, 21
  ILD, 31
  lung pathology, 15
  obstructive ventilatory defects, 16, 17*t*
  pre-surgical assessment, 22
  primary parameters, 13, 14
  quality rating scale, 118
  restriction, 142–145
  restrictive ventilatory defect, 29–30
  shape, flow–volume curve, 18–19

spirometry (*continued*)
interpretation, 17, 17*f*, 21
test quality, 13, 14*f*, 15*f*
TLC, 15, 16
tracheomalacia, 35
upper airway obstruction, 20–21, 20*f*
ventilatory function patterns, 15, 16*t*
vocal cord pathology, 36
static lung volume (SLV)
application, 41
asthma, 44–45
cardiomyopathy, respiratory assessment, 43–44
comparisons, 40–41
COPD, 41–42, 49–52
interstitial lung disease, HRCT, 46–47
non-specific ventilatory pattern, 39, 40
obesity hypoventilation syndrome, 48–49
parameters, 38
plethysmography, 37
sarcoidosis, 47–48
test quality, 37–38
and TLC, 59
ULN, 38–39, 39*f*, 40*t*
ventilatory function, spirometry and TLC, 39, 40
washout and dilution methods, 37
SVC. *See* slow vital capacity (SVC)

TLC. *See* total lung capacity (TLC)
total lung capacity (TLC)
and FVC, 16
morbid obesity, 49
neuromuscular disease, 57
reduced, 82
and SLV, 59
spirometry, 39
static lung volume measured, 15–16
and ULN, 38

ULN. *See* upper limit of normal (ULN)
upper airway obstruction, 20–21
upper limit of normal (ULN), 3, 38–39, 43

vasculitis, 139–142

wheeze, 111, 112, 158–159

Uploaded by [StormRG]

WILEY END USER LICENSE AGREEMENT

Go to www.wiley.com/go/eula to access Wiley’s ebook EULA.